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The purpose of the research is to characterize patterns of care, utilization, and outcomes of treatments for localized prostate cancer such as surgery, external beam radiation, and brachytherapy. In particular, the research characterizes the patterns of care, utilization and outcomes of minimally invasive radical prostatectomy (MIRP) versus open retropubic radical prostatectomy (RRP). MIRP utilization increased from 9% to 43% from 2003 to 2007. Lengths of stay, transfusions, and stricture rates are lower for MIRP vs. RRP. However, erectile dysfunction and incontinence were more frequently diagnosed postoperatively. Additionally positive surgical margins were similar by surgical approach. While higher RRP surgeon volume was associated with fewer complications, this was not observed for MIRP surgeon volume and outcomes. In addition, MIRP was $293 more costly than RRP. Finally, pelvic lymph node dissection was performed less frequently with MIRP vs. RRP.

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Table of Contents

I Introduction

The objective of this 4-year study is to characterize the use and outcomes of competing therapies for treating localized prostate cancer. Moreover, this project will evaluate utilization trends, patterns of care, costs and outcomes of minimally invasive radical prostatectomy (MIRP), i.e. laparoscopic radical prostatectomy (LRP) and robotic assisted laparoscopic radical prostatectomy (RALP), compared to open radical prostatectomy (ORP), external beam radiotherapy (XRT), and brachytherapy (BRCY). The findings of this project will guide men with prostate cancer weighing treatment options, employers and policy makers implementing healthcare coverage, and providers seeking to deliver cost-effective, high quality care. This project will be the first national, population-based study to evaluate patterns of care and outcomes for treatments of localized prostate cancer in a wide range of health care settings. In particular, we will assess the impact of LRP, RALP, XRT, and BRCY provider volume on complications, HRQOL, and cancer control, for which data is currently unavailable.

Body

One of our aims is to evaluate patterns of care and utilization trends for minimally invasive radical prostatectomy (MIRP). Using SEER-Medicare linked data during 2003-2007, we identified underwent 1938 MIRP vs. 6899 open retropubic radical prostatectomy (RRP), the gold standard surgical approach. Despite little evidence demonstrating superiority over RRP, MIRP utilization increased from 9.2% (95% confidence interval [CI], 8.1%-10.5%) in 2003 to 43.2% (95% CI, 39.6% - 46.9%) in 2006-2007.[1] In addition, we observed racial disparities, as men undergoing MIRP vs. RRP were more likely to be Asian (6.1% vs. 3.2%), less likely to be recorded as black (6.2% vs. 7.8%) or Hispanic (5.6% vs. 7.9%). Moreover, there were socio-demographic differences in terms of access to care, as men undergoing MIRP vs. RRP were more likely to reside in areas with at least 90% high school graduation rates (50.2% vs. 41.0%) and with median incomes of at least $60 000 (35.8% vs. 21.5%) (all $p<0.001$).

We also compared outcomes of MIRP vs. RRP. In propensity score–adjusted analyses, MIRP vs. RRP was associated with shorter length of stay (median, 2.0 vs., 3.0 days; $p<0.001$) and lower rates of blood transfusions (2.7% vs. 20.8%, $p<0.001$), postoperative respiratory complications (4.3% vs. 6.6%; $p=0.004$), miscellaneous surgical complications (4.3% vs. 5.6%; $p=0.03$), and anastomotic stricture (5.8% vs. 14.0%; $p<0.001$). However, MIRP vs. RRP was associated with an increased risk of genitourinary complications (4.7% vs. 2.1%; $P=0.001$) and diagnoses of incontinence (15.9 vs. 12.2 per 100 person-years; $p=0.02$) and erectile dysfunction (26.8 vs. 19.2 per 100 person-years; $p=.0009$). Rates of use of additional cancer therapies did not differ by

surgical procedure (8.2 vs. 6.9 per 100 person years; p=0.035). This contrasted with a prior study that we performed that showed greater use of radiation and hormones after MIRP.[2]

Two possibilities explain these findings; either MIRP technology inherently compromised functional outcomes, or surgeons had yet to fully master MIRP instrumentation during early, rapid adoption.[3] According to Intuitive Surgical, 600 press clippings accentuated MIRP negatives rather than positives and many patients and urologists may be misled by headlines and sound bytes without appreciating the findings within the framework of the study design. While SEER-Medicare lacks the granularity to determine nerve-sparing technique and validated instrument evaluation of incontinence and ED, it allows a population-based comparison of MIRP vs. RRP outcomes for surgeons whose findings might otherwise go unpublished. This is relevant, as >70% of radical prostatectomies are performed by low-volume surgeons.[4] While we adjusted for surgeon volume during our study period in sub-analyses, the administrative code for MIRP was initiated in 2003, and we were unable to adjust for surgeon experience prior to 2003. Moreover, adjusting for surgeon volume does not capture formal training in RRP vs. learn-on-the-fly MIRP experience, and there is tremendous heterogeneity in individual techniques and outcomes. Our comparative effectiveness study is akin to comparing mean scores of professionally instructed golfers and/or those with >20 years of experience vs. mostly self-taught beginners.

In the analyses of MIPR vs. RRP described above, we excluded men undergoing perineal radical prostatectomy (PRP) due to it becoming a infrequently use open surgical approach. However, for much of the 20th century, PRP was the predominant surgical approach. However, sampling pelvic lymph nodes involved a separate incision during PRP and urologists were using a lower midline for bladder, ureteral, and other pelvic surgeries more frequently. This led to a shift away from the perineal approach to the open retropubic approach, and due to loss of familiarity, PRP currently has a very prolonged learning curve. However, one could argue that minimally invasive approaches to radical prostatectomy have a very prolonged learning curve as well. The purpose of our population-based study was to compare cost and outcomes for PRP vs. RRP and MIRP.

We identified men who underwent PRP (n=452), MIRP (n=1,938), and RRP (n=6,899) during 2003 to 2007 from SEER-Medicare linked data, and PRP comprised 4.9% of the radical prostatectomies during the study period.[5] In propensity-score adjusted analyses, men undergoing PRP vs. RRP experienced shorter hospitalizations (median 2 vs. 3 days, $p<0.001$), fewer heterologous transfusions (7.2% vs. 20.8%, $p<0.001$), and required less additional cancer therapy (4.9% vs. 6.9%, $p=0.020$). When comparing PRP vs. MIRP, men undergoing PRP required more heterologous transfusions (7.2% vs. 2.7%, $p=0.018$), but experienced fewer miscellaneous medical complications (5.3% vs. 10.0%, $p=0.045$). The median expenditures for PRP, RRP, and MIRP were $11,019, $12,767, and $13,335 in the first six months post-operatively; therefore PRP cost $2,000 less than either RRP or MIRP ($p<0.001$).

This is the first population-based study comparing all 3 surgical approaches to radical prostatectomy, and despite its decreasing utilization in a nationally representative cohort in the last decade, PRP has equivalent or improved 30-day and intermediate and long-term outcomes compared with both open radical retropubic and minimally-invasive approaches to radical prostatectomy. With increased scrutiny on medical costs and comparative effectiveness, it appears that PRP offers an excellent option in the armamentarium of the urologist in treatment of prostate cancer. However, the decreasing utilization and lack of familiarity with this procedure in modern practice may limit the future application of this cost-effective and oncologically-sound approach to radical prostatectomy.

For radiation treatment of prostate cancer, intensity modulated radiation therapy (IMRT), a more costly treatment option compared to standard conformal radiation therapy (CRT), has been rapidly adopted with little evidence similar to MIRP for surgery. However, the cost implications for the rapid adoption of these technologies remains unclear in the U.S. health care system, which is saddled with spiraling health care costs and calls for reform. Using SEER–Medicare linked data, we determined treatment patterns for 45,636 men aged ≥65 years who received definitive surgery or radiation for localized prostate cancer diagnosed from 2002-2005.[6] We calculated costs attributable to prostate cancer as the difference in Medicare payments in the year following vs. the year prior to diagnosis, and all costs were standardized to 2008 dollars. Of the study cohort, 26% received surgery, 38% external bean radiotherapy, and 36% brachytherapy. Among surgical patients, MIRP utilization increased substantially (1.5% among 2002 diagnoses vs. 28.7% among 2005 diagnoses, $p<0.001$). For radiotherapy, IMRT utilization

increased substantially (28.7% vs. 81.7%, p<0.001) and for men receiving brachytherapy, supplemental IMRT increased significantly (8.5% vs. 31.1%, p<0.001). The mean incremental cost of IMRT vs. 3D-CRT was $10,986; of brachytherapy + IMRT vs. brachytherapy+3D-CRT was $10,789; of MIRP vs. open RP was $293. Extrapolating these figures to the total U.S. population results in excess spending of $282 million for IMRT, $59 million for brachytherapy+IMRT, and $4 million for MIRP, compared to less costly alternatives for men diagnosed in 2005.

Costlier prostate cancer therapies were rapidly and widely adopted, resulting in an excess national spending of over $350 million among men diagnosed in 2005 and suggesting the need for comparative effectiveness research to weigh their costs against their benefits, as there is little level I evidence, or population-based comparisons of these treatment modalities.

A measure of cancer control during radical prostatectomy is the likelihood of cancer at the edge of the specimen, or a positive surgical margin PSM. There are few comparisons of MIRP vs. RRP PSMs, and we used a population-based approach employing SEER-Medicare data to assess factors associated with PSMs.[7] Overall, 19.4% of men experienced PSMs with a pT2 vs. pT3a PSM rate of 14.9% vs. 42% (p<0.001). Extrapolating from our population-based results, a surgeon incurring more than 3 PSMs in 10 cases of pT2 disease performed below the 25th percentile. Additionally, there was a trend for fewer PSMs with minimally invasive vs. open RP (17.4% vs. 20.1%, p=0.086), and the PSM rate also decreased over the study period from 21.3% to 16.6% in 2004 vs. 2006 (p=0.028) with significant geographic variation (p<0.001). In adjusted analyses,

temporal and geographic variation in PSM persisted, and men with high (OR3.68, 95%CI 2.82-4.81) and intermediate (OR 2.52, 95%CI 2.03-3.13) vs. low-risk disease were at greater odds to experience PSMs. Notably, neither surgical approach nor surgeon volume was significantly associated with PSMs.

Our population-based PSM benchmarks allow identification of under-performing outliers who may seek courses or video self-study to improve outcomes. While there was significant temporal and geographic variation in PSMs, neither surgeon volume nor surgical approach was associated with PSMs. This is the first population-based study of PSMs during radical prostatectomy, which increases the likelihood of cancer recurrence and need for additional cancer therapies. In addition, we derived a means of identifying surgeons performing at or below the 25^{th} and 10^{th} percentiles, which may serve as a quality indicator for surgeons performing radical prostatectomy.

In assessing characteristics associated with the use of additional cancer therapies such as radiation and/or hormones after radical prostatectomy, we used SEER-Medicare data from 2004-2006 to identify 4,247 men who underwent RP, of whom 600 subsequently received adjuvant therapies.[8] We used Cox regression to identify factors associated with receipt of adjuvant therapies and estimate healthcare expenditures within 12 months of diagnosis were compared for RP alone vs. RP and adjuvant therapies. Biopsy Gleason score, PSA, risk group and SEER region were significantly associated with receipt of adjuvant treatments (all $p<0.001$). Higher surgeon volume was associated with lower odds of receiving adjuvant therapies (hazard ratio [HR], 0.60; 95%CI, 0.46-0.78 [$p<0.001$]). Factors associated with receipt of adjuvant therapies were positive

surgical margins (HR, 3.02; 95% CI, 2.55-3.57 [p<0.001]), high risk group vs. low (HR, 7.65; 95% CI, 5.64-10.37 [p<0.001]), lymph node positive disease (HR, 5.36; 95% CI, 3.71-7.75 [p<0.001]) and treatment in Iowa (HR, 1.93; 95%CI, 1.12-3.32 [p=0.019]) and New Mexico/Georgia/Hawaii (HR, 1.92; 95%CI, 1.09-3.39 [p=0.025]) vs. San Francisco SEER regions. Age, race, comorbidities, and surgical approach were not associated with use of adjuvant therapies. The median expenditures attributable to post-prostatectomy hormonal therapy, radiation therapy, and radiation with hormonal therapy vs. were $3,697, $17,290, and $29,385.

Men treated by high volume surgeons were less likely to receive adjuvant therapies. Regional variation and high-risk disease characteristics were associated with increased receipt of adjuvant therapies, which increased health expenditures by 2-3 fold when radiotherapy was administered. This study reinforces the importance of limiting positive surgical margins, which increase the cost of treating prostate cancer if adjuvant or salvage radiation or hormone therapy is added.

Higher RRP surgeon volume is associated with lower complications and shorter lengths of stay. However, the effect of MIRP surgeon volume on outcome is less clear. Therefore we performed a population-based study to determine the effect of MIRP surgeon volume on outcomes, and correlate with those of RRP surgeon volume-outcomes.[9] We identified 8,831 men who undergoing MIRP and RRP by 1,457 low, medium, and high volume surgeons from SEER-Medicare linked data from 2003 to 2007. After stratifying by surgeon RRP and MIRP volume, the following outcomes were studied: length of stay, transfusions, post-operative 30-day and anastomotic stricture

complications, and use of additional cancer therapies. Men undergoing MIRP with high and medium vs. low volume surgeons were less likely to require additional cancer therapies (4.5% and 4.7% vs. 7%, $p< 0.020$). Similarly, men undergoing RRP with high vs. medium and low volume surgeons were less likely to require additional cancer therapies (5.7% vs. 6.8% and 7.1%, $p<0.044$). Men undergoing ORP with high vs. medium and low volume surgeons experienced shorter lengths of stay (2.9 vs. 3.3 and 3.6 days, $p<0.001$), and fewer transfusions (15.4% vs. 21.3% and 22.7%, $p<0.017$), 30-day complications (18.4% vs. 25.6% and 25.7%, $p<0.001$), and anastomotic strictures (10.1% vs. 15.6% and 16.3%, $p<0.003$). However, MIRP surgeon volume did not affect these outcomes.

Men undergoing MIRP or ORP with high volume surgeons were less likely to require additional cancer therapies. Additionally, patients of high volume ORP surgeons were more likely to experience shorter hospital stays, fewer transfusions, 30-day complications, and anastomotic strictures, while MIRP surgeon volume did not affect these peri-operative outcomes. This data along with the temporal difference in introduction and diffusion of technique suggests that MIRP surgical technique is evolving in contrast to ORP technique, which has matured.

A pelvic lymph node dissection (PLND) is performed during radical prostatectomy for staging purposes to determine whether prostate cancer has metastasized. We also compared the likelihood of performing a PLND by surgical approach and assessed for characteristics associated with performing pelvic lymph node dissection.[10] PLND was performed for 87.6% vs. 38.3% of men undergoing RRP vs.

MIRP ($p<0.001$). Among men undergoing RRP, 82.6 vs. 4.6% underwent extended vs. limited PLND with a median yield of 4 vs. 3 lymph nodes ($p<0.001$). Additionally, the median MIRP PLND yield was 3 lymph nodes. In adjusted analyses, men undergoing RRP vs. MIRP (odds ratio [OR] 16.7; 95% confidence interval [CI], 11.1-25.0), those with few vs. multiple comorbidities (OR 1.4, 95%CI 1.02-1.91), intermediate (OR 1.87; 95%CI 1.48-2.37) and high (OR 2.77; 95%CI 2.02-3.78) vs. low risk features, and men treated by high volume surgeons (OR 1.008; 95%CI 1.004-1.011) were more likely to undergo PLND. Conversely, Hispanic (OR 0.68, 95%CI 0.49-0.96) vs. white men were less likely to undergo PLND.

Independent of tumor indices, men undergoing RRP vs. MIRP were more likely to undergo PLND with greater lymph node yield. This suggests that non-clinical factors influence surgeon practice patterns regarding PLND, and PLND overutilization may be driven by financial incentives to the surgeons. Further studies are needed to determine the appropriate utilization of PLND for men with prostate cancer.

In assessing patterns of care for men with prostate cancer, we also examined factors associated with the use of pretreatment imaging for men with low-risk prostate cancer. At present, pre-treatment imaging is only recommended for high-risk prostate cancer, and there is a less than 1% risk for a positive bone scan or computerized tomography (CT) scan. Using SEER-Medicare data from 2004-2005, we identified 6,444 men low with low-risk prostate cancer, and 2,330 (36.2%) underwent imaging studies; 1512 (23.5%), 1710 (26.5%), and 118 (1.8%) men underwent cross-sectional imaging (CT or MRI), bone scan, and abdominal ultrasound, respectively.[11] Radiation therapy vs.

surgery was associated with greater odds of imaging (Odds Ratio [OR], 1.99; 95% CI, 1.68-2.35 [p<0.01]). While active surveillance vs. surgery was associated with lower odds of imaging (OR, 0.44; 95% CI, 0.34-0.56 [p<0.01]). Factors associated with increased odds of imaging were median household income > $60,000 (OR, 1.41; 95% CI, 1.11-1.79 [p<0.01]), and men from New Jersey vs. San Francisco (OR, 3.11; 95% CI 2.24-4.33 [p<0.01]) experienced greater odds of imaging. Men living in areas with >90% vs. <75% high school education experienced lower odds imaging (OR, 0.76; 95% CI, 0.6-0.95 [p=0.02]). There is widespread overutilization and significant geographic variation for use of imaging to stage low-risk prostate cancer. Moreover, treatment associated variation in imaging was noted with the greatest vs. lowest imaging utilization observed for radiation therapy vs. active surveillance.

Challenges of our research are as follows. First, we sought to differentiate robotic-assisted laparoscopic radical prostatectomy from standard laparoscopic radical prostatectomy with use of the Healthcare Common Procedure Coding System (HCPCS) code S2900. However, our queries of SEER-Medicare data did not result in any men having this designation. We learned that Medicare does not reimburse a facility fee for use of the robot, and this may be why we have been unable to find this designation. Our alternative approach to this is evaluate the Healthcare Costs and Utilization Project (HCUP) Nationwide Inpatient Sample to use the ICD-9 code 17.44, which was initiated on 10/1/08. We are therefore purchasing NIS data for 2009, which will become available in 3/1/2011.

The second challenge has been the evaluation of urinary continence and erectile dysfunction following treatments for localized prostate cancer. Originally, we proposed to conduct a survey of Medicare beneficiaries; however, the cost estimate from RESDAC underestimated the survey costs. Moreover, the limitations of a survey of Medicare beneficiaries are that we will not have designation of nerve-sparing or robotic-assistance for radical prostatectomy. Moreover, preservation of continence and potency are most challenging in men aged 65 years and older. As an alternative approach, I have contacted the New Jersey and Northern California Cancer SEER registries to perform a survey of men who were treated for prostate cancer in those regions. However, the budget for contacting and performing a survey of these men will be more expensive that the original budget. We will therefore compare the utilization, outcomes, and costs of incontinence and erectile dysfunction following treatments for localized prostate cancer using SEER-Medicare and NIS data.

Finally, current manuscripts target include an assessment of the effect of surgeon and hospital volume on radical prostatectomy costs. In addition, the most recent release of Medicare Part D data will allow us to assess the use of medications and associated costs following minimally invasive versus open radical prostatectomy. We are also conducting an analysis of cryotherapy as a treatment option for prostate cancer compared to ablative therapies such as brachytherapy. Moreover, we are also assessing under-imaging utilization for prostate cancer prior to treatment. Additionally, we are assessing the efficacy and outcomes for adjuvant and salvage radiation therapy following radical prostatectomy.

Key Research Accomplishments

- First population-based comparison of MIRP vs. RRP. Due to the absence of randomized-control trials, this is presently the most inclusive study on this controversial topic. There were also more than 600 press articles about this paper in JAMA.
- First population-based comparison of PRP to RRP and MIRP that demonstrated that PRP is less costly and has similar or better outcomes compared to PRP and MIRP. PRP was abandoned to due lack of familiarity with this operative approach and therefore a prolonged learning curve. However, many open surgeons face unfamiliar anatomy and a prolonged learning curve when transitioning from RRP to MIRP.
- We also published the rapid adoption of IMRT in the Journal of Clinical Oncology, which has not been documented. We show that the adoption of IMRT and MIRP over less costly "traditional" therapies resulted in Medicare costs of $345 million in 2005. This cost is much greater when considering the number of men treated for prostate cancer that are younger than 65 years, and the greater reimbursement of private insurances relative to Medicare.
- Using population-based data, we described PSMs for pT2 (organ confined prostate cancer) and pT3a (extracapsular extension). Prior PSMs come largely from single surgeon case series, which may not be generalizable to community health settings. We also established a means for identifying underperforming surgeons, the bottom 25^{th} and 10^{th} percentiles, such that these surgeons can

recognize and improve upon these suboptimal outcomes through video study or courses.

- We characterized the expense of adjuvant therapies for prostate cancer after radical prostatectomy, such as radiation and/or hormonal therapy. The use of these therapies is likely to increase, given recent data from randomized control trials that demonstrate improved biochemical and overall survival from early adjuvant radiation therapy.
- We demonstrate the increased utilization of PLND during RRP vs. MIRP, and the overutilization of PLND, as current guidelines recommend PLND for men with high-risk disease. Conformance with guidelines would lead to decreased cost of care and improved quality, given the low likelihood of lymph node positive disease for men with low and intermediate risk disease.
- Finally, we identified over-utilization of imaging (MRI, CT and bone scan) among men with newly diagnosed prostate cancer. Similar to PLND, conformance to guidelines will decrease spending and improve quality of care given the low risk of metastases in men with low-risk prostate cancer.

Reportable Outcomes

The Prostate Cancer Physician Training Award has resulted in publications in the following journals:

JAMA

Journal of Urology

British Journal of Urology

Cancer (In Press)

Journal of Clinical Oncology (In Press)

Urology

Urologic Oncology

In addition, 4 abstracts were presented at the American Urologic Association in 2010 in San Francisco and 1 abstract the American Society for Clinical Oncology in 2010.

Conclusions

The study to date is the first population-based comparison of MIRP vs. RRP, and is the highest level of evidence, as randomized control trials are lacking and are unlikely to be performed. Despite the absence of firm evidence, men of greater education and income were more likely to undergo MIRP vs. RRP. In addition, racial disparities were noted, as whites and Asians vs. Blacks and Hispanics were more likely to undergo MIRP. In addition, our study on MIRP vs. RRP surgeon volume outcomes effects suggests that MIRP is not yet a mature technique compared to RRP, given the absence of an association of better MIRP outcomes with higher MIRP surgeon volume. In addition, we present population-based surgeon PSMs to help identify underperforming surgeons and also characterize the increased cost associated with adjuvant or salvage hormonal therapy. Finally, we characterized the additional health care costs of rapid, unregulated adoption of MIRP and IMRT and the overutilization of imaging for men with low-risk prostate cancer and the overutilization of PLND during radical prostatectomy. These may serve as potential areas to greater educate physicians and to dis-incentivize unnecessary imaging studies and surgeries.

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Appendices

Utilization and Expense of Adjuvant Cancer Therapies Following Radical Prostatectomy

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ABSTRACT

BACKGROUND: We sought to identify factors associated with the use of adjuvant therapies and its costs following radical prostatectomy (RP).

METHODS: We used SEER-Medicare data from 2004-2006 to identify 4,247 men who underwent RP, of whom 600 subsequently received adjuvant therapies. We used Cox regression to identify factors associated with receipt of adjuvant therapies. Healthcare expenditures within 12 months of diagnosis were compared for RP alone vs. RP and adjuvant therapies.

RESULTS: Biopsy Gleason score, PSA, risk group and SEER region were significantly associated with receipt of adjuvant treatments (all p<0.001). Higher surgeon volume was associated with lower odds of receiving adjuvant therapies (hazard ratio [HR], 0.60; 95%CI, 0.46-0.78 [p<0.001]). Factors associated with receipt of adjuvant therapies were positive surgical margins (HR, 3.02; 95% CI, 2.55-3.57 [p<0.001]), high risk group vs. low (HR, 7.65; 95% CI, 5.64-10.37 [p<0.001]), lymph node positive disease (HR, 5.36; 95% CI, 3.71-7.75 [p<0.001]) and treatment in Iowa (HR, 1.93; 95%CI, 1.12-3.32 [p=0.019]) and New Mexico/Georgia/Hawaii (HR, 1.92; 95%CI, 1.09-3.39 [p=0.025]) vs. San Francisco SEER regions. Age, race, comorbidities, and surgical approach were not associated with use of adjuvant therapies. The median expenditures attributable to post-prostatectomy hormonal therapy, radiation therapy, and radiation with hormonal therapy vs. were $3,697, $17,290, and $29,385.

CONCLUSIONS: Men treated by high volume surgeons were less likely to

receive adjuvant therapies. Regional variation and high-risk disease characteristicswere associated with increased receipt of adjuvant therapies, which increased health expenditures by 2-3 fold when radiotherapy was administered.

INTRODUCTION

Prostate cancer remains the most common solid organ tumor among U.S. men with approximately 192,000 incident cases in 2009.[12] The majority of these tumors are localized and radical prostatectomy (RP) remains the most popular treatment option.[13] However, 21% to 37% of men experience biochemical recurrence (BCR) after radical prostatectomy.[14] Recent studies have shown that post-prostatectomy radiotherapy improves prostate cancer specific survival[15] and significantly decreases overall mortality when used in the adjuvant[16] or salvage setting in selected men with high risk disease.[17] Furthermore, the benefit of hormonal therapy needs to be carefully balanced against the significant inherent risks of cardiovascular and thromboembolic disease with the substantial health care costs of implementing this treatment.[18-20] Hormonal therapy as it pertains to the adjuvant setting, whether or not in combination with radiotherapy, has been less extensively evaluated with no definitive guidelines on who and when to initiate treatment.[19,20]

While there are few contemporary characterizations of secondary therapies,[17,21,22] a study of Medicare beneficiaries from the early 1990s demonstrated 35% of men receive secondary therapies following radical prostatectomy.[23] However, this may not reflect contemporary practice patterns due to the downward stage migration that followed the advent of PSA screening.[24] The purpose of our population-based study was to evaluate factors

associated with the use of adjuvant cancer therapies following radical prostatectomy and estimate the associated health care expenditures of these treatments.

MATERIALS AND METHODS

Data

Our study was approved by the Brigham and Women's Institutional Review Board; patient data were de-identified and the requirement for consent was waived. We used Surveillance, Epidemiology, and End Results (SEER)–Medicare data for analysis, which is comprised of a linkage of population-based cancer registry data from 16 SEER areas with Medicare administrative data and covers approximately 26% of the U.S. population. The Medicare program provides benefits to 97% of Americans aged ≥65 years.[25]

Study Cohort

We identified 4,247 men aged ≥65 years, diagnosed with prostate cancer in 2004 and 2005 who underwent radical prostatectomy through 2006 based on Physicians Current Procedural Terminology Coding System 4th edition, (CPT-4): 55840, 55842, 55845 for open radical prostatectomy; and 55866 for minimally invasive radical prostatectomy. CPT-4 code 55899 (unspecified male

genitourinary procedure) may sometimes be used with an open radical prostatectomy administrative code to specify minimally invasive radical prostatectomy with robotic assistance for private health plans[26], but Medicare does not recognize this coding schema, and very few men had this combination of codes; therefore, this was not used to identify minimally invasive radical prostatectomy. We excluded men not enrolled in both Medicare Part A and B, or who were enrolled in a Medicare health maintenance organization (because their claims are not reliably submitted). Because SEER only captures positive margin characteristics for American Joint Commission on Cancer (AJCC) pathologic T2 and T3a disease, we excluded 292 men with pathologic stage T3b, 63 men with pathologic T4, and 412 men with missing margin status from our cohort. Men with lymph node positive disease (n=45) were included in the study. Additionally, to increase the sensitivity for detecting additional postoperative radiation therapy, we restricted our cohort to men with prostate cancer diagnosed as their only cancer. A total of 204 patients with other cancers including non-melanoma skin cancers were excluded from the analysis.

Outcomes

We examined the utilization of secondary therapy (radiation and/or hormonal) after radical prostatectomy in men with pathologic T2 and T3a disease.[2,23] According to the American Urological Association (AUA) 2007 guidelines, additional radiation and/or hormonal therapy should be administered to men with adverse pathologic features and/or positive surgical margins.[27] Administrative

codes defining adjuvant therapy and the individual components of radiation and hormonal therapy are listed in the Appendix.

Control Variables

Age was obtained from the Medicare file; race, census tract measures of median household income and high school education, region, population density (urban vs. rural), and marital status were obtained from SEER registry data. Comorbidity was assessed using the Klabunde modification of the Charlson index during the year before surgery.[28] The Klabunde modification uses comorbid conditions identified by the Charlson comorbidity index and incorporates the diagnostic and procedure data contained in Medicare physician (Part B) claims. Variables were categorized as in Table 1. Additionally, we used PSA, Gleason Grade, and clinical stage to stratify men to low, intermediate, and high-risk disease.[29] However, tumor stage was missing/unknown for almost one third of our subjects, and we therefore used a modified risk stratification without clinical stage, resulting in a low risk designation for 29% of our cohort. Therefore, we used a modified risk classification defined as follows: PSA<10 and biopsy Gleason score <7 = low, PSA 10-20 or Gleason score 7 = intermediate, PSA >20 or Gleason score >7 = high.

Because surgeon rather than hospital volume is the more significant determinant of outcomes following open radical prostatectomy [30], we determined surgeon volume for each type of procedure by aggregating the number of procedures performed from 2004-06. Surgeon volume was categorized into quartiles, consistent with a prior study.[31]

Expenditures Related to the Use of Secondary Cancer Therapies

We compared baseline health care expenditures in the 12 months prior to prostate cancer diagnosis for men who underwent radical prostatectomy alone vs. those who underwent adjuvant treatment post-prostatectomy. To determine the total expense of adjuvant treatment, we summed the total healthcare expenditures from the beneficiary, Medicare, and supplemental private insurance for inpatient, outpatient, and physician services within 12 months of prostate cancer diagnosis. To ensure that we adequately captured the cost of treatment, we excluded men who underwent radical prostatectomy and secondary therapies beyond 6 months following prostate cancer diagnosis. We then subtracted baseline health care expenditures, allowing subjects to serve as their own controls. We considered the difference in health expenditures between men receiving adjuvant treatment vs. radical prostatectomy alone to be the health care expenditures attributable to hormonal therapy, radiotherapy, and both treatments in combination. Moreover, the health care expenditures includes therapies, consultations, imaging, laboratory tests, and treatment of

complications. All costs were adjusted to 2008 dollars using the 2007 Annual Report of the Boards of Trustees of the Federal Hospital Insurance and Federal Supplementary Medical Insurance Trust Fund.[32]

Statistical Analysis

Unadjusted analysis using the Pearson chi-square statistic was performed to compare demographic and biopsy tumor characteristics for men receiving adjuvant treatmentvs. radical prostatectomy alone, adjusting for clustering by surgeon, surgical approach, surgeon volume, and pathologic features.[33] A two-sided result of $p<0.05$ was considered statistically significant. Adjusted analysis was performed with a Cox multivariable regression model to assess the association of the covariates on the use of adjuvanttherapies.

All tests were considered statistically significant at $\alpha=0.05$. All analyses were performed with SAS version 9.1.3 (SAS Institute, Cary, NC).

RESULTS

The demographics of our study population are summarized in Table 1. We observed a temporal trend in the administration of adjuvant therapy after radical prostatectomy; men were more likely to receive adjuvant therapy after radical

prostatectomy performed in 2004 vs. 2005 or 2006 (15.5%, 13.7% and 10.5%, p=0.028). Moreover, while age, comorbidities, income, and education were not associated with receipt of adjuvant therapies, there was significant geographic variation for utilization of adjuvant therapies with San Jose vs. Detroit region having the highest vs. lowest utilization rates (20.4% vs. 9.9%, p<0.001). Furthermore, more aggressive tumor characteristics (higher Gleason grade, pre-operative PSA, and risk-stratification) were associated with receipt of adjuvant cancer therapy (all p<0.001).

In assessing the effect of surgical approach, surgeon volume, and pathologic features on the use of adjuvant therapies (Table 2), men undergoing MIRP vs. RRP were less likely to receive additional cancer therapy (10.9% vs. 15.3%, p<0.001), and higher surgeon volume was associated with lower utilization of adjuvant cancer therapy (p=0.001). Moreover, men with pathologic stage T3a vs. T2 disease were more likely to receive additional therapy (36.4% vs. 9.7%, p<0.001), and men with positive vs. negative surgical margins were more likely to receive adjuvant cancer therapy (31.5% vs. 10.0%, p<0.001). Finally, men with positie lymph nodes were more likely to receive additional therapy (75.6% vs. 13.5%, p<0.001).

In adjusted analysis (Table 3), age, race, marital status, and surgical approach (MIRP vs. RRP) were not significantly associated with receipt of adjuvant therapies. However, risk stratification was significantly associated with use of adjuvant therapies as men with intermediate (HR, 2.86; 95% CI, 2.14-3.83 [p<0.001]) and high (HR, 7.65; 5.64-10.37 [p<0.001]) vs. low risk disease experienced 3 and 8 times greater rate of receiving adjuvant therapies, respectively. Men undergoing radical prostatectomy by very high volume surgeons were less likely to receive adjuvant therapies (HR, 0.60; 95% CI, 0.46-0.78 [p<0.001]). Moreover, men with positive vs. negative surgical margins experienced 3 times greater rate of receiving adjuvant therapies (HR, 3.02; 95%CI, 2.55-3.57 [p<0.001]). Men with positive versus negative lymph nodes were 5 times more likely to receive adjuvant therapies (HR, 5.36; 95%CI, 3.71-7.75 [p<0.001]). Additionally, there was greater use of adjuvant therapies in Iowa (HR, 1.93; 95%CI, 1.12-3.32 [p=0.019]) and New Mexico/Georgia/Hawaii (HR, 1.92; 95%CI, 1.09-3.39 [p=0.025]) vs. San Francisco SEER regions.

Baseline healthcare expenditures in the 12 months prior to prostate cancer diagnosis did not differ for men who underwent radical prostatectomy alone vs. adjuvant therapies of hormonal therapy, radiation therapy, and hormone and radiation therapy. As expected, the 12-month post-prostate cancer diagnosis healthcare expenditures (Table 4) of men who underwent radical prostatectomy alone vs. adjuvant therapies of hormonal therapy, radiation therapy, and

combination hormonal and radiation therapy were significantly greater for adjuvant therapies ($p<0.001$).

DISCUSSION

Approximately 13% to 34% of men who undergo prostatectomy will have adverse pathologic features such as positive surgical margins or extracapsular extension/pT3a disease.[34,35] There is a lack of consensus regarding when to initiate treatment in such men, however, 22% to 34% of these men will receive salvage secondary treatments within 3 years of BCR.[36,37] While, a recent population-based study demonstrated significantly greater use of additional cancer treatments, i.e. radiation and/or hormonal therapy, within 6 months of minimally invasive vs. open radical prostatectomy, potential confounders such as surgical margin status and pathologic stage and grade were unavailable in this analysis of Medicare beneficiaries.[2] Additionally, there is an absence of population-based studies that assess use of secondary treatments after adjusting for surgical approach and surgeon volume. Aside from the lack of definitive guidelines on when to initiate secondary treatments after BCR and the appropriateness thereof, there is also concern of the added healthcare costs when secondary therapies are initiated.

Our paper has several important findings. First, higher surgeon volume was associated with decreased utilization of adjuvant cancer therapy independent of

tumor characteristics. These findings would suggest that heterogeneity in practice patterns exist and that there is not uniform standardization of care. More experienced surgeons may prefer to manage positive surgical margins and extracapsular extension conservatively with surveillance vs. adjuvant therapy. Similarly, Bianco et al. found significant heterogeneity among BCR rates after adjusting for tumor characteristics and surgeon experience, and oncologic outcomes vary due to measured and unmeasured characteristics of the treating surgeon.[38] Thus, as Bianco et al. alluded to, there must be unmeasured characteristics of high volume surgeons that result in decreased use of secondary therapies.

Second, we found that risk stratification was a significant predictor of adjuvant therapy use. Intermediate to high risk patients were approximately 3 to 8 times more likely to receive adjuvant therapy. Tumor biology as measured by pathologic stage and grade have been previously shown to be powerful predictors for additional cancer therapy, whereas other patient variables including age and comorbidity have not.[23] Moreover, rapid prostate-specific antigen doubling time has also been shown to be significant predictors for secondary therapies.[39] Unfortunately, these endpoints are not captured in SEER-Medicare.

Third, positive surgical margin status was associated with increased utilization of adjuvant therapies despite mixed evidence available during our study period regarding the impact of positive surgical margins on cancer recurrence and survival.[40] However, recently published randomized control trials demonstrate survival benefit from early adjuvant radiotherapy for positive surgical margins and high-risk features.[16,41] The interpretation of these trials is not without ongoing controversy and further studies are warranted to clarify which patients would benefit most from adjuvant treatment.[42] Furthermore, patients with lymph node positive disease were more likely to receive adjuvant therapy. Although controversial, this increase in utilization of adjuvant therapy in lymph node positive patients may be explained by prior studies which have shown improved cancer specific survival in such patients managed with adjuvant therapy.[43,44] With greater dissemination of evidence in favor of early adjuvant radiotherapy for adverse pathologic features, more widespread adjuvant therapy use is expected and our results may underestimate current and future utilization of secondary therapies as practice patterns evolve.

Fourth, patient age, comorbidity status and race were not significant predictors of adjuvant cancer therapy consistent with prior studies.[22,23,39]. One would expect that patient factors such as older age and more comorbidities would decrease the likelihood of receiving adjuvant therapies if treatment decisions were individualized. Moreover, these findings may highlight the need for guidelines

based on life-expectancy and post-prostatectomy nomograms to better stratify which men benefit most from adjuvant therapy. Additionally, surgical approach was not a significant predictor for adjuvant therapy in the multivariate analysis. Our findings contradict other studies which demonstrated greater use of secondary therapies following minimally invasive vs. open radical prostatectomy while the other found no difference. [1,2] This difference may result from differences between the study populations: a 5% random sample of Medicare beneficiaries[2] vs. 100% of the Medicare beneficiaries in SEER tumor registry regions. Our study captures the entire surgeon Medicare experience in SEER regions vs. a national 5% sampling of surgeon Medicare experience.

Finally, health care expenditures were $29,385 higher for combination radiation and hormonal therapy vs. no treatment following prostatectomy. The additional expenditures for adjuvant hormonal therapy and radiotherapy were $3,697 and $17,290, respectively vs. radical prostatectomy alone. In particular, positive surgical margins, a surgeon dependent variable, may increase the cost of cancer therapy significantly, particularly after level 1 evidence of improved survival from secondary radiation therapy.[15,16,17]

Our findings must be interpreted in the context of the study design. First, Medicare is limited to men aged 65 years and older, and nerve-sparing may be performed more frequently in younger, potent men.[45] This, along with the absence of margin status for pathologic T3b and T4 disease, may lead to

underestimation of the overall prevalence of secondary cancer treatments in men undergoing radical prostatectomy.[34] Second, the SEER tumor registry does not contain detailed clinical information on PSA or biochemical recurrence, tumor volume, perineural invasion, and tertiary high Gleason grade, factors that increase the likelihood adjuvant therapy utilization.[46-48] Third, we were unable to determine whether adjuvant radiotherapy was administered in an adjuvant vs. salvage fashion because post-prostatectomy PSA was unavailable. This is noteworthy because initiation of adjuvant adjuvant therapies is influenced by variation in provider practice patterns while initiation of salvage therapy may be influenced by variations in PSA biochemical recurrence thresholds. Finally, our estimates of adjuvant therapy expenditures are lower than expenditures by private health plans vs. Medicare.

CONCLUSION

Higher surgeon volume and geographic variation was independently associated with decrease utilization of additional therapy, demonstrating physician and regional practice pattern heterogeneity. Men undergoing radical prostatectomy were significantly more likely to undergo adjuvant treatments in the presence of higher risk stratification and positive surgical margins. Finally, adjuvant therapies significantly increased cancer specific health care expenditures by 2-3 fold when radiotherapy was administered postoperatively.

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INTRODUCTION

Prostate cancer remains the most common solid organ tumor among U.S. men with approximately 192,000 incident cases in 2009.[12] The majority of these tumors are localized and radical prostatectomy (RP) remains the most popular treatment option.[13] However, 21% to 37% of men experience biochemical recurrence (BCR) after radical prostatectomy.[14] Recent studies have shown that post-prostatectomy radiotherapy improves prostate cancer specific survival[15] and significantly decreases overall mortality when used in the adjuvant[16] or salvage setting in selected men with high risk disease.[17] Furthermore, the benefit of hormonal therapy needs to be carefully balanced against the significant inherent risks of cardiovascular and thromboembolic disease with the substantial health care costs of implementing this treatment.[18-20] Hormonal therapy as it pertains to the adjuvant setting, whether or not in combination with radiotherapy, has been less extensively evaluated with no definitive guidelines on who and when to initiate treatment.[19,20]

While there are few contemporary characterizations of secondary therapies,[17,21,22] a study of Medicare beneficiaries from the early 1990s demonstrated 35% of men receive secondary therapies following radical prostatectomy.[23] However, this may not reflect contemporary practice patterns due to the downward stage migration that followed the advent of PSA screening.[24] The purpose of our population-based study was to evaluate factors

associated with the use of adjuvant cancer therapies following radical prostatectomy and estimate the associated health care expenditures of these treatments.

MATERIALS AND METHODS

Data

Our study was approved by the Brigham and Women's Institutional Review Board; patient data were de-identified and the requirement for consent was waived. We used Surveillance, Epidemiology, and End Results (SEER)–Medicare data for analysis, which is comprised of a linkage of population-based cancer registry data from 16 SEER areas with Medicare administrative data and covers approximately 26% of the U.S. population. The Medicare program provides benefits to 97% of Americans aged ≥65 years.[25]

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genitourinary procedure) may sometimes be used with an open radical prostatectomy administrative code to specify minimally invasive radical prostatectomy with robotic assistance for private health plans[26], but Medicare does not recognize this coding schema, and very few men had this combination of codes; therefore, this was not used to identify minimally invasive radical prostatectomy. We excluded men not enrolled in both Medicare Part A and B, or who were enrolled in a Medicare health maintenance organization (because their claims are not reliably submitted). Because SEER only captures positive margin characteristics for American Joint Commission on Cancer (AJCC) pathologic T2 and T3a disease, we excluded 292 men with pathologic stage T3b, 63 men with pathologic T4, and 412 men with missing margin status from our cohort. Men with lymph node positive disease (n=45) were included in the study. Additionally, to increase the sensitivity for detecting additional postoperative radiation therapy, we restricted our cohort to men with prostate cancer diagnosed as their only cancer. A total of 204 patients with other cancers including non-melanoma skin cancers were excluded from the analysis.

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We examined the utilization of secondary therapy (radiation and/or hormonal) after radical prostatectomy in men with pathologic T2 and T3a disease.[2,23] According to the American Urological Association (AUA) 2007 guidelines, additional radiation and/or hormonal therapy should be administered to men with adverse pathologic features and/or positive surgical margins.[27] Administrative

codes defining adjuvant therapy and the individual components of radiation and hormonal therapy are listed in the Appendix.

Control Variables

Age was obtained from the Medicare file; race, census tract measures of median household income and high school education, region, population density (urban vs. rural), and marital status were obtained from SEER registry data. Comorbidity was assessed using the Klabunde modification of the Charlson index during the year before surgery.[28] The Klabunde modification uses comorbid conditions identified by the Charlson comorbidity index and incorporates the diagnostic and procedure data contained in Medicare physician (Part B) claims. Variables were categorized as in Table 1. Additionally, we used PSA, Gleason Grade, and clinical stage to stratify men to low, intermediate, and high-risk disease.[29] However, tumor stage was missing/unknown for almost one third of our subjects, and we therefore used a modified risk stratification without clinical stage, resulting in a low risk designation for 29% of our cohort. Therefore, we used a modified risk classification defined as follows: PSA<10 and biopsy Gleason score <7 = low, PSA 10-20 or Gleason score 7 = intermediate, PSA >20 or Gleason score >7 = high.

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complications. All costs were adjusted to 2008 dollars using the 2007 Annual Report of the Boards of Trustees of the Federal Hospital Insurance and Federal Supplementary Medical Insurance Trust Fund.[32]

Statistical Analysis

Unadjusted analysis using the Pearson chi-square statistic was performed to compare demographic and biopsy tumor characteristics for men receiving adjuvant treatmentvs. radical prostatectomy alone, adjusting for clustering by surgeon, surgical approach, surgeon volume, and pathologic features.[33] A two-sided result of $p<0.05$ was considered statistically significant. Adjusted analysis was performed with a Cox multivariable regression model to assess the association of the covariates on the use of adjuvanttherapies.

All tests were considered statistically significant at $\alpha=0.05$. All analyses were performed with SAS version 9.1.3 (SAS Institute, Cary, NC).

RESULTS

The demographics of our study population are summarized in Table 1. We observed a temporal trend in the administration of adjuvant therapy after radical prostatectomy; men were more likely to receive adjuvant therapy after radical

prostatectomy performed in 2004 vs. 2005 or 2006 (15.5%, 13.7% and 10.5%, p=0.028). Moreover, while age, comorbidities, income, and education were not associated with receipt of adjuvant therapies, there was significant geographic variation for utilization of adjuvant therapies with San Jose vs. Detroit region having the highest vs. lowest utilization rates (20.4% vs. 9.9%, p<0.001). Furthermore, more aggressive tumor characteristics (higher Gleason grade, pre-operative PSA, and risk-stratification) were associated with receipt of adjuvant cancer therapy (all p<0.001).

In assessing the effect of surgical approach, surgeon volume, and pathologic features on the use of adjuvant therapies (Table 2), men undergoing MIRP vs. RRP were less likely to receive additional cancer therapy (10.9% vs. 15.3%, p<0.001), and higher surgeon volume was associated with lower utilization of adjuvant cancer therapy (p=0.001). Moreover, men with pathologic stage T3a vs. T2 disease were more likely to receive additional therapy (36.4% vs. 9.7%, p<0.001), and men with positive vs. negative surgical margins were more likely to receive adjuvant cancer therapy (31.5% vs. 10.0%, p<0.001). Finally, men with positie lymph nodes were more likely to receive additional therapy (75.6% vs. 13.5%, p<0.001).

In adjusted analysis (Table 3), age, race, marital status, and surgical approach (MIRP vs. RRP) were not significantly associated with receipt of adjuvant therapies. However, risk stratification was significantly associated with use of adjuvant therapies as men with intermediate (HR, 2.86; 95% CI, 2.14-3.83 [p<0.001]) and high (HR, 7.65; 5.64-10.37 [p<0.001]) vs. low risk disease experienced 3 and 8 times greater rate of receiving adjuvant therapies, respectively. Men undergoing radical prostatectomy by very high volume surgeons were less likely to receive adjuvant therapies (HR, 0.60; 95% CI, 0.46-0.78 [p<0.001]). Moreover, men with positive vs. negative surgical margins experienced 3 times greater rate of receiving adjuvant therapies (HR, 3.02; 95%CI, 2.55-3.57 [p<0.001]). Men with positive versus negative lymph nodes were 5 times more likely to receive adjuvant therapies (HR, 5.36; 95%CI, 3.71-7.75 [p<0.001]). Additionally, there was greater use of adjuvant therapies in Iowa (HR, 1.93; 95%CI, 1.12-3.32 [p=0.019]) and New Mexico/Georgia/Hawaii (HR, 1.92; 95%CI, 1.09-3.39 [p=0.025]) vs. San Francisco SEER regions.

Baseline healthcare expenditures in the 12 months prior to prostate cancer diagnosis did not differ for men who underwent radical prostatectomy alone vs. adjuvant therapies of hormonal therapy, radiation therapy, and hormone and radiation therapy. As expected, the 12-month post-prostate cancer diagnosis healthcare expenditures (Table 4) of men who underwent radical prostatectomy alone vs. adjuvant therapies of hormonal therapy, radiation therapy, and

combination hormonal and radiation therapy were significantly greater for adjuvant therapies ($p<0.001$).

DISCUSSION

Approximately 13% to 34% of men who undergo prostatectomy will have adverse pathologic features such as positive surgical margins or extracapsular extension/pT3a disease.[34,35] There is a lack of consensus regarding when to initiate treatment in such men, however, 22% to 34% of these men will receive salvage secondary treatments within 3 years of BCR.[36,37] While, a recent population-based study demonstrated significantly greater use of additional cancer treatments, i.e. radiation and/or hormonal therapy, within 6 months of minimally invasive vs. open radical prostatectomy, potential confounders such as surgical margin status and pathologic stage and grade were unavailable in this analysis of Medicare beneficiaries.[2] Additionally, there is an absence of population-based studies that assess use of secondary treatments after adjusting for surgical approach and surgeon volume. Aside from the lack of definitive guidelines on when to initiate secondary treatments after BCR and the appropriateness thereof, there is also concern of the added healthcare costs when secondary therapies are initiated.

Our paper has several important findings. First, higher surgeon volume was associated with decreased utilization of adjuvant cancer therapy independent of

tumor characteristics. These findings would suggest that heterogeneity in practice patterns exist and that there is not uniform standardization of care. More experienced surgeons may prefer to manage positive surgical margins and extracapsular extension conservatively with surveillance vs. adjuvant therapy. Similarly, Bianco et al. found significant heterogeneity among BCR rates after adjusting for tumor characteristics and surgeon experience, and oncologic outcomes vary due to measured and unmeasured characteristics of the treating surgeon.[38] Thus, as Bianco et al. alluded to, there must be unmeasured characteristics of high volume surgeons that result in decreased use of secondary therapies.

Second, we found that risk stratification was a significant predictor of adjuvant therapy use. Intermediate to high risk patients were approximately 3 to 8 times more likely to receive adjuvant therapy. Tumor biology as measured by pathologic stage and grade have been previously shown to be powerful predictors for additional cancer therapy, whereas other patient variables including age and comorbidity have not.[23] Moreover, rapid prostate-specific antigen doubling time has also been shown to be significant predictors for secondary therapies.[39] Unfortunately, these endpoints are not captured in SEER-Medicare.

Third, positive surgical margin status was associated with increased utilization of adjuvant therapies despite mixed evidence available during our study period regarding the impact of positive surgical margins on cancer recurrence and survival.[40] However, recently published randomized control trials demonstrate survival benefit from early adjuvant radiotherapy for positive surgical margins and high-risk features.[16,41] The interpretation of these trials is not without ongoing controversy and further studies are warranted to clarify which patients would benefit most from adjuvant treatment.[42] Furthermore, patients with lymph node positive disease were more likely to receive adjuvant therapy. Although controversial, this increase in utilization of adjuvant therapy in lymph node positive patients may be explained by prior studies which have shown improved cancer specific survival in such patients managed with adjuvant therapy.[43,44] With greater dissemination of evidence in favor of early adjuvant radiotherapy for adverse pathologic features, more widespread adjuvant therapy use is expected and our results may underestimate current and future utilization of secondary therapies as practice patterns evolve.

Fourth, patient age, comorbidity status and race were not significant predictors of adjuvant cancer therapy consistent with prior studies.[22,23,39]. One would expect that patient factors such as older age and more comorbidities would decrease the likelihood of receiving adjuvant therapies if treatment decisions were individualized. Moreover, these findings may highlight the need for guidelines

based on life-expectancy and post-prostatectomy nomograms to better stratify which men benefit most from adjuvant therapy. Additionally, surgical approach was not a significant predictor for adjuvant therapy in the multivariate analysis. Our findings contradict other studies which demonstrated greater use of secondary therapies following minimally invasive vs. open radical prostatectomy while the other found no difference. [1,2] This difference may result from differences between the study populations: a 5% random sample of Medicare beneficiaries[2] vs. 100% of the Medicare beneficiaries in SEER tumor registry regions. Our study captures the entire surgeon Medicare experience in SEER regions vs. a national 5% sampling of surgeon Medicare experience.

Finally, health care expenditures were $29,385 higher for combination radiation and hormonal therapy vs. no treatment following prostatectomy. The additional expenditures for adjuvant hormonal therapy and radiotherapy were $3,697 and $17,290, respectively vs. radical prostatectomy alone. In particular, positive surgical margins, a surgeon dependent variable, may increase the cost of cancer therapy significantly, particularly after level 1 evidence of improved survival from secondary radiation therapy.[15,16,17]

Our findings must be interpreted in the context of the study design. First, Medicare is limited to men aged 65 years and older, and nerve-sparing may be performed more frequently in younger, potent men.[45] This, along with the absence of margin status for pathologic T3b and T4 disease, may lead to

underestimation of the overall prevalence of secondary cancer treatments in men undergoing radical prostatectomy.[34] Second, the SEER tumor registry does not contain detailed clinical information on PSA or biochemical recurrence, tumor volume, perineural invasion, and tertiary high Gleason grade, factors that increase the likelihood adjuvant therapy utilization.[46-48] Third, we were unable to determine whether adjuvant radiotherapy was administered in an adjuvant vs. salvage fashion because post-prostatectomy PSA was unavailable. This is noteworthy because initiation of adjuvant adjuvant therapies is influenced by variation in provider practice patterns while initiation of salvage therapy may be influenced by variations in PSA biochemical recurrence thresholds. Finally, our estimates of adjuvant therapy expenditures are lower than expenditures by private health plans vs. Medicare.

CONCLUSION

Higher surgeon volume and geographic variation was independently associated with decrease utilization of additional therapy, demonstrating physician and regional practice pattern heterogeneity. Men undergoing radical prostatectomy were significantly more likely to undergo adjuvant treatments in the presence of higher risk stratification and positive surgical margins. Finally, adjuvant therapies significantly increased cancer specific health care expenditures by 2-3 fold when radiotherapy was administered postoperatively.

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Utilization and Expense of Adjuvant Cancer Therapies Following Radical Prostatectomy

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ABSTRACT

BACKGROUND: We sought to identify factors associated with the use of adjuvant therapies and its costs following radical prostatectomy (RP).

METHODS: We used SEER-Medicare data from 2004-2006 to identify 4,247 men who underwent RP, of whom 600 subsequently received adjuvant therapies. We used Cox regression to identify factors associated with receipt of adjuvant therapies. Healthcare expenditures within 12 months of diagnosis were compared for RP alone vs. RP and adjuvant therapies.

RESULTS: Biopsy Gleason score, PSA, risk group and SEER region were significantly associated with receipt of adjuvant treatments (all p<0.001). Higher surgeon volume was associated with lower odds of receiving adjuvant therapies (hazard ratio [HR], 0.60; 95%CI, 0.46-0.78 [p<0.001]). Factors associated with receipt of adjuvant therapies were positive surgical margins (HR, 3.02; 95% CI, 2.55-3.57 [p<0.001]), high risk group vs. low (HR, 7.65; 95% CI, 5.64-10.37 [p<0.001]), lymph node positive disease (HR, 5.36; 95% CI, 3.71-7.75 [p<0.001]) and treatment in Iowa (HR, 1.93; 95%CI, 1.12-3.32 [p=0.019]) and New Mexico/Georgia/Hawaii (HR, 1.92; 95%CI, 1.09-3.39 [p=0.025]) vs. San Francisco SEER regions. Age, race, comorbidities, and surgical approach were not associated with use of adjuvant therapies. The median expenditures attributable to post-prostatectomy hormonal therapy, radiation therapy, and radiation with hormonal therapy vs. were $3,697, $17,290, and $29,385.

CONCLUSIONS: Men treated by high volume surgeons were less likely to

receive adjuvant therapies. Regional variation and high-risk disease characteristicswere associated with increased receipt of adjuvant therapies, which increased health expenditures by 2-3 fold when radiotherapy was administered.

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The demographics of our study population are summarized in Table 1. We observed a temporal trend in the administration of adjuvant therapy after radical prostatectomy; men were more likely to receive adjuvant therapy after radical

prostatectomy performed in 2004 vs. 2005 or 2006 (15.5%, 13.7% and 10.5%, p=0.028). Moreover, while age, comorbidities, income, and education were not associated with receipt of adjuvant therapies, there was significant geographic variation for utilization of adjuvant therapies with San Jose vs. Detroit region having the highest vs. lowest utilization rates (20.4% vs. 9.9%, p<0.001). Furthermore, more aggressive tumor characteristics (higher Gleason grade, pre-operative PSA, and risk-stratification) were associated with receipt of adjuvant cancer therapy (all p<0.001).

In assessing the effect of surgical approach, surgeon volume, and pathologic features on the use of adjuvant therapies (Table 2), men undergoing MIRP vs. RRP were less likely to receive additional cancer therapy (10.9% vs. 15.3%, p<0.001), and higher surgeon volume was associated with lower utilization of adjuvant cancer therapy (p=0.001). Moreover, men with pathologic stage T3a vs. T2 disease were more likely to receive additional therapy (36.4% vs. 9.7%, p<0.001), and men with positive vs. negative surgical margins were more likely to receive adjuvant cancer therapy (31.5% vs. 10.0%, p<0.001). Finally, men with positie lymph nodes were more likely to receive additional therapy (75.6% vs. 13.5%, p<0.001).

In adjusted analysis (Table 3), age, race, marital status, and surgical approach (MIRP vs. RRP) were not significantly associated with receipt of adjuvant therapies. However, risk stratification was significantly associated with use of adjuvant therapies as men with intermediate (HR, 2.86; 95% CI, 2.14-3.83 [p<0.001]) and high (HR, 7.65; 5.64-10.37 [p<0.001]) vs. low risk disease experienced 3 and 8 times greater rate of receiving adjuvant therapies, respectively. Men undergoing radical prostatectomy by very high volume surgeons were less likely to receive adjuvant therapies (HR, 0.60; 95% CI, 0.46-0.78 [p<0.001]). Moreover, men with positive vs. negative surgical margins experienced 3 times greater rate of receiving adjuvant therapies (HR, 3.02; 95%CI, 2.55-3.57 [p<0.001]). Men with positive versus negative lymph nodes were 5 times more likely to receive adjuvant therapies (HR, 5.36; 95%CI, 3.71-7.75 [p<0.001]). Additionally, there was greater use of adjuvant therapies in Iowa (HR, 1.93; 95%CI, 1.12-3.32 [p=0.019]) and New Mexico/Georgia/Hawaii (HR, 1.92; 95%CI, 1.09-3.39 [p=0.025]) vs. San Francisco SEER regions.

Baseline healthcare expenditures in the 12 months prior to prostate cancer diagnosis did not differ for men who underwent radical prostatectomy alone vs. adjuvant therapies of hormonal therapy, radiation therapy, and hormone and radiation therapy. As expected, the 12-month post-prostate cancer diagnosis healthcare expenditures (Table 4) of men who underwent radical prostatectomy alone vs. adjuvant therapies of hormonal therapy, radiation therapy, and

combination hormonal and radiation therapy were significantly greater for adjuvant therapies ($p<0.001$).

DISCUSSION

Approximately 13% to 34% of men who undergo prostatectomy will have adverse pathologic features such as positive surgical margins or extracapsular extension/pT3a disease.[34,35] There is a lack of consensus regarding when to initiate treatment in such men, however, 22% to 34% of these men will receive salvage secondary treatments within 3 years of BCR.[36,37] While, a recent population-based study demonstrated significantly greater use of additional cancer treatments, i.e. radiation and/or hormonal therapy, within 6 months of minimally invasive vs. open radical prostatectomy, potential confounders such as surgical margin status and pathologic stage and grade were unavailable in this analysis of Medicare beneficiaries.[2] Additionally, there is an absence of population-based studies that assess use of secondary treatments after adjusting for surgical approach and surgeon volume. Aside from the lack of definitive guidelines on when to initiate secondary treatments after BCR and the appropriateness thereof, there is also concern of the added healthcare costs when secondary therapies are initiated.

Our paper has several important findings. First, higher surgeon volume was associated with decreased utilization of adjuvant cancer therapy independent of

tumor characteristics. These findings would suggest that heterogeneity in practice patterns exist and that there is not uniform standardization of care. More experienced surgeons may prefer to manage positive surgical margins and extracapsular extension conservatively with surveillance vs. adjuvant therapy. Similarly, Bianco et al. found significant heterogeneity among BCR rates after adjusting for tumor characteristics and surgeon experience, and oncologic outcomes vary due to measured and unmeasured characteristics of the treating surgeon.[38] Thus, as Bianco et al. alluded to, there must be unmeasured characteristics of high volume surgeons that result in decreased use of secondary therapies.

Second, we found that risk stratification was a significant predictor of adjuvant therapy use. Intermediate to high risk patients were approximately 3 to 8 times more likely to receive adjuvant therapy. Tumor biology as measured by pathologic stage and grade have been previously shown to be powerful predictors for additional cancer therapy, whereas other patient variables including age and comorbidity have not.[23] Moreover, rapid prostate-specific antigen doubling time has also been shown to be significant predictors for secondary therapies.[39] Unfortunately, these endpoints are not captured in SEER-Medicare.

Third, positive surgical margin status was associated with increased utilization of adjuvant therapies despite mixed evidence available during our study period regarding the impact of positive surgical margins on cancer recurrence and survival.[40] However, recently published randomized control trials demonstrate survival benefit from early adjuvant radiotherapy for positive surgical margins and high-risk features.[16,41] The interpretation of these trials is not without ongoing controversy and further studies are warranted to clarify which patients would benefit most from adjuvant treatment.[42] Furthermore, patients with lymph node positive disease were more likely to receive adjuvant therapy. Although controversial, this increase in utilization of adjuvant therapy in lymph node positive patients may be explained by prior studies which have shown improved cancer specific survival in such patients managed with adjuvant therapy.[43,44] With greater dissemination of evidence in favor of early adjuvant radiotherapy for adverse pathologic features, more widespread adjuvant therapy use is expected and our results may underestimate current and future utilization of secondary therapies as practice patterns evolve.

Fourth, patient age, comorbidity status and race were not significant predictors of adjuvant cancer therapy consistent with prior studies.[22,23,39]. One would expect that patient factors such as older age and more comorbidities would decrease the likelihood of receiving adjuvant therapies if treatment decisions were individualized. Moreover, these findings may highlight the need for guidelines

based on life-expectancy and post-prostatectomy nomograms to better stratify which men benefit most from adjuvant therapy. Additionally, surgical approach was not a significant predictor for adjuvant therapy in the multivariate analysis. Our findings contradict other studies which demonstrated greater use of secondary therapies following minimally invasive vs. open radical prostatectomy while the other found no difference. [1,2] This difference may result from differences between the study populations: a 5% random sample of Medicare beneficiaries[2] vs. 100% of the Medicare beneficiaries in SEER tumor registry regions. Our study captures the entire surgeon Medicare experience in SEER regions vs. a national 5% sampling of surgeon Medicare experience.

Finally, health care expenditures were $29,385 higher for combination radiation and hormonal therapy vs. no treatment following prostatectomy. The additional expenditures for adjuvant hormonal therapy and radiotherapy were $3,697 and $17,290, respectively vs. radical prostatectomy alone. In particular, positive surgical margins, a surgeon dependent variable, may increase the cost of cancer therapy significantly, particularly after level 1 evidence of improved survival from secondary radiation therapy.[15,16,17]

Our findings must be interpreted in the context of the study design. First, Medicare is limited to men aged 65 years and older, and nerve-sparing may be performed more frequently in younger, potent men.[45] This, along with the absence of margin status for pathologic T3b and T4 disease, may lead to

underestimation of the overall prevalence of secondary cancer treatments in men undergoing radical prostatectomy.[34] Second, the SEER tumor registry does not contain detailed clinical information on PSA or biochemical recurrence, tumor volume, perineural invasion, and tertiary high Gleason grade, factors that increase the likelihood adjuvant therapy utilization.[46-48] Third, we were unable to determine whether adjuvant radiotherapy was administered in an adjuvant vs. salvage fashion because post-prostatectomy PSA was unavailable. This is noteworthy because initiation of adjuvant adjuvant therapies is influenced by variation in provider practice patterns while initiation of salvage therapy may be influenced by variations in PSA biochemical recurrence thresholds. Finally, our estimates of adjuvant therapy expenditures are lower than expenditures by private health plans vs. Medicare.

CONCLUSION

Higher surgeon volume and geographic variation was independently associated with decrease utilization of additional therapy, demonstrating physician and regional practice pattern heterogeneity. Men undergoing radical prostatectomy were significantly more likely to undergo adjuvant treatments in the presence of higher risk stratification and positive surgical margins. Finally, adjuvant therapies significantly increased cancer specific health care expenditures by 2-3 fold when radiotherapy was administered postoperatively.

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Comparative Effectiveness of Minimally Invasive vs Open Radical Prostatectomy

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Context Minimally invasive radical prostatectomy (MIRP) has diffused rapidly despite limited data on outcomes and greater costs compared with open retropubic radical prostatectomy (RRP).

Objective To determine the comparative effectiveness of MIRP vs RRP.

Design, Setting, and Patients Population-based observational cohort study using US Surveillance, Epidemiology, and End Results Medicare linked data from 2003 through 2007. We identified men with prostate cancer who underwent MIRP (n=1938) vs RRP (n=6899).

Main Outcome Measures We compared postoperative 30-day complications, anastomotic stricture 31 to 365 days postoperatively, long-term incontinence and erectile dysfunction more than 18 months postoperatively, and postoperative use of additional cancer therapies, a surrogate for cancer control.

Results Among men undergoing prostatectomy, use of MIRP increased from 9.2% (95% confidence interval [CI], 8.1%-10.5%) in 2003 to 43.2% (95% CI, 39.6%-46.9%) in 2006-2007. Men undergoing MIRP vs RRP were more likely to be recorded as Asian (6.1% vs 3.2%), less likely to be recorded as black (6.2% vs 7.8%) or Hispanic (5.6% vs 7.9%), and more likely to live in areas with at least 90% high school graduation rates (50.2% vs 41.0%) and with median incomes of at least $60 000 (35.8% vs 21.5%) (all $P<.001$). In propensity score–adjusted analyses, MIRP vs RRP was associated with shorter length of stay (median, 2.0 vs 3.0 days; $P<.001$) and lower rates of blood transfusions (2.7% vs 20.8%; $P<.001$), postoperative respiratory complications (4.3% vs 6.6%; $P=.004$), miscellaneous surgical complications (4.3% vs 5.6%; $P=.03$), and anastomotic stricture (5.8% vs 14.0%; $P<.001$). However, MIRP vs RRP was associated with an increased risk of genitourinary complications (4.7% vs 2.1%; $P=.001$) and diagnoses of incontinence (15.9 vs 12.2 per 100 person-years; $P=.02$) and erectile dysfunction (26.8 vs 19.2 per 100 person-years; $P=.009$). Rates of use of additional cancer therapies did not differ by surgical procedure (8.2 vs 6.9 per 100 person-years; $P=.35$).

Conclusion Men undergoing MIRP vs RRP experienced shorter length of stay, fewer respiratory and miscellaneous surgical complications and strictures, and similar postoperative use of additional cancer therapies but experienced more genitourinary complications, incontinence, and erectile dysfunction.

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FOLLOWING THE DESCRIPTION OF consistently reproducible advantages of minimally invasive radical prostatectomy (MIRP) with and without robotic assistance in 2000-2001,[1,2] use of MIRP has surged.[3,4] In particular, use of robotic-assisted MIRP increased from 1% to 40% of all radical prostatectomies from 2001 to 2006.[5,6] Many patients intuitively perceive minimally invasive approaches to reduce complications compared with conventional open operations and prefer minimally invasive procedures because of smaller incisions requiring less analgesics and shorter hospital stays, even at greater cost.[7]

Moreover, the widespread direct-to-consumer advertising and marketed benefits of robotic-assisted MIRP in the United States may promote publication bias against studies that detail challenges and suboptimal outcomes early in the MIRP learning curve.[8] Until comparative effectiveness of robotic-assisted MIRP can be demonstrated, open retropubic radical prostatectomy (RRP), with a 20-year lead time for dissemination of surgical technique[9] relative to MIRP, remains the gold standard surgical therapy for localized prostate cancer.[10]

For surgeons eager to add robotic-assisted MIRP to their armamentarium, there are few barriers to entry; surgeons must attend a 2-day course before scheduling cases proctored by another surgeon who has performed at least 20 robotic-assisted MIRPs. Requirements may be less rigorous for attaining hospital privileges for MIRP without robotic assistance. Studies estimate the learning curve for either approach to be at least 150 to 250 cases,[11,12] and greater RRP or MIRP sur-

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geon volume is associated with better outcomes.[4,13-15]

In the absence of randomized controlled trials, population-based studies allow comparison of competing therapies across a broad range of health settings. The aim of our study was to assess outcomes following MIRP vs RRP.

METHODS

Data

Our study was approved by the Brigham and Women's Institutional Review Board; patient data were deidentified and the requirement for consent was waived. We used Surveillance, Epidemiology, and End Results (SEER)–Medicare data for analyses,[16] which are composed of a linkage of population-based cancer registry data from 16 SEER areas covering approximately 26% of the US population with Medicare administrative data. The Medicare program provides benefits to most Americans aged 65 years or older.

Study Cohort

We identified 137 217 men aged 65 years or older who were diagnosed as having prostate cancer from 2002 to 2005 and followed up through December 31, 2007. We excluded 10 441 men who were enrolled in a health maintenance organization or who were not enrolled in both Medicare Part A and Part B throughout the duration of the study (because claims are not reliably submitted for such patients). To increase the sensitivity for detection of postoperative radiation therapy, we restricted our analyses to men with prostate cancer diagnosed as their first and only cancer and excluded 8271 men with other cancers. We excluded 452 men who underwent an open perineal radical prostatectomy because this approach was used infrequently (4.9% of radical prostatectomies during our study period) and differs in surgical incision, anatomic approach, and outcomes from RRP and MIRP,[17,18] and we performed a sensitivity analysis that revealed differences in perineal radical prostatectomy vs RRP outcomes.

We then identified the study cohort of 8837 men who underwent radical prostatectomy from January 1, 2003, through December 31, 2007. Radical prostatectomy was identified from Medicare inpatient, outpatient, and carrier component files (formerly Physician/Provider B files) based on the presence of Current Procedural Terminology, Fourth Edition (CPT-4) codes 55840, 55842, and 55845 for RRP (n=6899) and 55866 for MIRP (n=1938).

The CPT-4 code 55899, unspecified male genitourinary procedure, may sometimes be used along with an RRP *International Classification of Diseases, Ninth Revision* code to specify MIRP with robotic assistance for private health plans.[19] Medicare does not recognize this variation in coding, and we identified very few men with this combination of codes; therefore, it was not used to ascertain MIRP.

Outcomes

We examined outcomes consistent with prior studies: mortality/morbidity, length of stay, anastomotic strictures, incontinence, erectile dysfunction, and additional cancer therapy[3,4,13,14,20-22] (eAppendix). Postoperative complications and transfusions were assessed in the 30 days after surgery. Complication categories included cardiac, respiratory, genitourinary, vascular, wound, and miscellaneous events. Postoperative mortality was defined as death within 30 days of radical prostatectomy.

Anastomotic strictures were assessed from 31 to 365 days after surgery.[13] Long-term diagnoses and procedures for incontinence[13] and erectile dysfunction[20,21] were assessed based on administrative data more than 18 months after surgery, the interim required for recovery of postoperative urinary and sexual function to plateau.[23] Therefore, men undergoing MIRP and RRP in the latter half of 2006 and 2007 were excluded from the assessment of postoperative functional outcomes.

We also identified men undergoing additional cancer therapy after prostatectomy consistent with prior studies[3,22] as a surrogate for cancer control. According to guidelines, additional radiation therapy, hormone therapy, or both should be administered after surgery if prostate-specific antigen levels fail to reach undetectable levels or for men with adverse pathologic features or positive surgical margins.[24] We documented overall additional cancer therapy and the individual components of radiation and hormone therapy.

Control Variables

Information on patient age was obtained from the Medicare file, while race/ethnicity (based on medical record review and supplemented with Hispanic surname matching), census tract measures of median household income and proportion of individuals with at least a high school education, SEER region, population density (urban vs rural), and marital status were obtained from SEER registry data. We examined race/ethnicity because we hypothesized that disparities may exist in patient access or self-selection for a novel marketed procedure without proven benefit compared with a gold standard. Because of small numbers, we combined the New Mexico, rural Georgia, and Atlanta SEER registries.

Comorbidity using the Klabunde modification of the Charlson index and preoperative diagnoses of incontinence and erectile dysfunction were captured based on inpatient, outpatient, and carrier claims during the year before surgery.[25] We controlled for baseline incontinence and erectile dysfunction in our adjusted analysis and also conducted a sensitivity analysis in which we excluded men with preexisting incontinence and erectile dysfunction and obtained similar results. Variables were categorized as in TABLE 1.

Because surgeon rather than hospital volume is the more significant determinant of outcomes following RRP,[14] we determined surgeon volume for each type of procedure by aggregating the number of procedures for all men in the cohort performed from 2003 through 2007. For men with more than

Table 1. Demographic and Tumor Characteristics of the Study Population[a]

Characteristics	Before Propensity Weighting			After Propensity Weighting[b]		
	MIRP (n = 1938)	RRP (n = 6899)	*P* Value	MIRP (n = 1938)	RRP (n = 6889)	*P* Value
Year of surgery[c]						
2003	244 (12.6)	2394 (34.7)	<.001	586 (30.2)	2059 (29.9)	>.99
2004	542 (28.0)	2218 (32.2)		600 (30.9)	2150 (31.2)	
2005	843 (43.5)	1881 (27.3)		604 (31.1)	2144 (31.1)	
2006	277 (14.3)	370 (5.4)		139 (7.1)	489 (7.1)	
2007	32 (1.7)	36 (0.5)		14 (0.7)	53 (0.8)	
Age, y						
65-69	1162 (60.0)	4351 (63.1)	.12	1209 (62.2)	4310 (62.5)	.97
70-74	626 (32.3)	2094 (30.4)		599 (30.8)	2119 (30.7)	
≥75	150 (7.7)	454 (6.6)		135 (7)	465 (6.7)	
Charlson comorbidity score						
0	1375 (71.0)	4704 (68.2)	.10	1295 (66.7)	4740 (68.7)	.50
1	430 (22.2)	1706 (24.7)		506 (26)	1667 (24.2)	
≥2	133 (6.9)	489 (7.1)		142 (7.3)	488 (7.1)	
Race/ethnicity						
White	1558 (80.4)	5514 (79.9)	.001	1496 (77)	5520 (80.1)	.60
Black	120 (6.2)	535 (7.8)		204 (10.5)	519 (7.5)	
Hispanic	109 (5.6)	547 (7.9)		143 (7.3)	512 (7.4)	
Asian	119 (6.1)	220 (3.2)		74 (3.8)	255 (3.7)	
Other	32 (1.7)	83 (1.2)		26 (1.3)	89 (1.3)	
Marital status						
Not married	261 (13.5)	1053 (15.3)	<.001	287 (14.8)	1031 (15)	.97
Married	1497 (77.2)	5528 (80.1)		1550 (79.8)	5471 (79.4)	
Unknown	180 (9.3)	318 (4.6)		106 (5.5)	392 (5.7)	
Residents in patient's census tract with at least a high school education, %						
<75	283 (14.6)	1381 (20.0)	<.001	364 (18.8)	1297 (18.8)	.86
75-84.9	354 (18.3)	1380 (20.0)		418 (21.5)	1356 (19.7)	
85-90	328 (16.9)	1309 (19.0)		352 (18.1)	1278 (18.5)	
>90	973 (50.2)	2827 (41.0)		808 (41.6)	2961 (43)	
Median household income in census tract of residence, $						
<35 000	359 (18.5)	2134 (30.9)	<.001	553 (28.5)	1947 (28.2)	.95
35 000-44 499	408 (21.1)	1662 (24.1)		475 (24.4)	1614 (23.4)	
45 000-59 999	477 (24.6)	1616 (23.4)		437 (22.5)	1636 (23.7)	
≥60 000	694 (35.8)	1485 (21.5)		478 (24.6)	1696 (24.6)	
SEER registry						
San Francisco	95 (4.9)	228 (3.3)	.01	82 (4.2)	258 (3.7)	>.99
Detroit	284 (14.7)	385 (5.6)		151 (7.8)	526 (7.6)	
Hawaii	41 (2.1)	63 (0.9)		19 (1)	74 (1.1)	
Iowa	53 (2.7)	461 (6.7)		119 (6.1)	403 (5.8)	
Seattle	101 (5.2)	643 (9.3)		122 (6.3)	575 (8.3)	
Utah	65 (3.4)	435 (6.3)		87 (4.5)	390 (5.7)	
Connecticut	61 (3.2)	267 (3.9)		67 (3.5)	257 (3.7)	
San Jose	50 (2.6)	149 (2.2)		60 (3.1)	160 (2.3)	
Los Angeles	262 (13.5)	719 (10.4)		212 (10.9)	759 (11)	
Greater California	519 (26.8)	1641 (23.8)		475 (24.4)	1679 (24.4)	
Kentucky	111 (5.7)	404 (5.9)		99 (5.1)	403 (5.9)	
Louisiana	84 (4.3)	603 (8.7)		152 (7.8)	536 (7.8)	
New Jersey	177 (9.1)	521 (7.6)		156 (8)	548 (8)	
New Mexico/Atlanta/rural Georgia	35 (1.8)	380 (5.5)		143 (7.4)	325 (4.7)	
Population density						
Metropolitan	1846 (95.3)	6292 (91.2)	.007	1821 (93.8)	6349 (92.1)	.33
Nonmetropolitan	92 (4.8)	607 (8.8)		121 (6.2)	545 (7.9)	

(continued)

Table 1. Demographic and Tumor Characteristics of the Study Population[a] (continued)

Characteristics	Before Propensity Weighting			After Propensity Weighting[b]		
	MIRP (n = 1938)	RRP (n = 6899)	*P* Value	MIRP (n = 1938)	RRP (n = 6889)	*P* Value
Baseline urinary incontinence	118 (6.1)	257 (3.7)	.007	77 (4)	299 (4.3)	.67
Baseline erectile dysfunction	441 (22.8)	773 (11.2)	<.001	261 (13.4)	948 (13.8)	.90
AJCC pathologic stage						
T2 (organ-confined)	1323 (68.3)	4196 (60.8)	<.001	1157 (59.6)	4306 (62.5)	.43
T3 (extracapsular or seminal vesicle invasion)	339 (17.5)	1733 (25.1)		438 (22.6)	1615 (23.4)	
T4 (invading bladder and/or rectum)	22 (1.1)	97 (1.4)		34 (1.7)	93 (1.4)	
Unknown	254 (13.1)	873 (12.7)		313 (16.1)	880 (12.8)	
Tumor grade						
Well-/moderately differentiated	947 (48.9)	3485 (50.5)	.59	962 (49.5)	3460 (50.2)	.95
Poorly/undifferentiated	979 (50.5)	3381 (49.0)		972 (50)	3400 (49.3)	
Unknown	12 (0.6)	33 (0.5)		9 (0.5)	34 (0.5)	

Abbreviations: AJCC, American Joint Committee on Cancer; MIRP, minimally invasive radical prostatectomy; RRP, open retropubic radical prostatectomy; SEER, Surveillance, Epidemiology, and End Results.
[a]Data are presented as No. (%) unless otherwise noted.
[b]Using propensity score weighting to balance all characteristics in the 2 groups based on all characteristics in the table.
[c]The study cohort included men diagnosed as having prostate cancer in 2002-2005 who underwent radical prostatectomy in 2003-2007.

1 surgeon listed, we selected the surgeon who performed the larger volume of radical prostatectomies for analysis.[13] We also adjusted for year of surgery because outcomes may improve over time.[20]

Statistical Analysis

Annual utilization rates for RRP and MIRP were derived, and temporal trends in use were compared using the Mantel-Haenszel χ^2 test for trend, adjusted for surgeon clustering. Because of the relatively smaller number of procedures performed in 2007, we combined procedure data from 2006 and 2007 for the analysis of temporal trends. For dichotomous outcomes occurring within a fixed time interval, such as 30-day outcomes and 31- to 365-day (anastomotic strictures) outcomes, we compared proportions (number of events divided by number of patients) for MIRP vs RRP. For outcome variables without an upper time bound, in which length of follow-up could vary (eg, use of additional cancer therapy, diagnosis or procedures for incontinence and erectile dysfunction), we compared rates (number of events per 100 person-years of follow-up) for MIRP vs RRP. We also compared median length of stay between groups.

Because men undergoing MIRP differed from those undergoing RRP in terms of demographic and tumor characteristics, we used weighted propensity score methods to adjust for these differences.[26,27] Propensity score methods permit control for observed confounding factors that might influence both group assignment and outcome using a single composite measure and attempts to balance patient characteristics between groups.

To conduct the propensity score adjustment, we used a logistic regression model to calculate the propensity (probability) of undergoing MIRP vs RRP based on all covariates described above and then weighted each patient's data based on the inverse propensity of being in 1 of the 2 treatment groups.[28] Covariate balance was checked after adjustment (Table 1). In secondary analyses, we repeated the propensity-adjusted comparisons including surgeon volume in the propensity score models to assess if differences in surgeon volume explained differences in the outcomes studied; however, no differences were observed, suggesting that surgeon volume does not explain the differences observed.

Generalized estimating equations[29] (GEEs) were used to account for surgeon clustering in both unadjusted and adjusted analyses. To compare unadjusted proportions, we fit GEE logistic regressions with surgical approach (MIRP vs RRP) as the only covariate. To compare unadjusted rates, we fit GEE log-linear Poisson regression[30,31] with surgical approach as the only covariate. The *P* value for significance of surgical approach is calculated from the GEE logistic regression and Poisson regression *z* tests. A GEE was used in which length of stay was modeled as log-normal to compare length of stay. The models for the adjusted vs unadjusted GEE analyses were identical except that each patient was weighted by the inverse of the propensity score in the adjusted GEE.

Missing data were infrequent (<5% on any variable). We performed additional analyses using various missing data statistical approaches including multiple imputation and weighted estimating equations.[32,33] The results changed very little, so we present the results analyzing missing data as a separate category. With 8837 men in our cohort and a 5% type I error, we had more than 80% power to detect an odds ratio (OR) of 1.97 for infrequent outcomes such as cardiac complications (using a GEE logistic regression *z* test) and to detect a rate ratio of 1.36 for more frequent outcomes such as erectile dysfunction (using a GEE Poisson regression *z* test). All tests were considered statistically significant at $\alpha = .05$.

All analyses were performed with SAS version 9.1.3 (SAS Institute Inc, Cary, North Carolina).

RESULTS

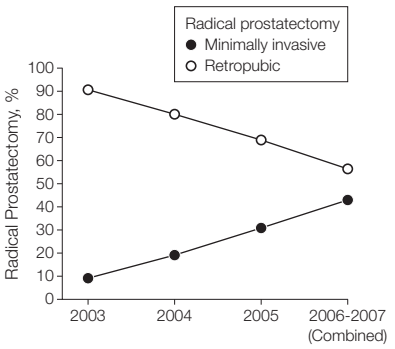
Among the 8837 men undergoing radical prostatectomy, use of MIRP increased almost 5-fold from 9.2% (95% confidence interval [CI], 8.1%-10.5%) in 2003 to 43.2% (95% CI, 39.6%-46.9%) in 2006-2007 (FIGURE). The number of surgeries performed in 2006 and 2007 appears to have decreased because data on new cancer diagnoses were available only through 2005. We observed sociodemographic differences among men undergoing MIRP vs RRP (Table 1). Relatively fewer men recorded as black (6.2% vs 7.8%) and Hispanic (5.6% vs 7.9%) underwent MIRP vs RRP, whereas those recorded as Asian were more likely (6.1% vs 3.2%) to undergo MIRP vs RRP ($P<.001$). In addition, men who underwent MIRP vs RRP were more likely to live in areas with at least 90% high school graduation rates (50.2% vs 41.0%) and median household income of at least $60 000 (35.8% vs 21.5%) (all $P<.001$).

We also observed geographic variation, with relatively greater use of MIRP vs RRP in the Detroit, Michigan (14.7% vs 5.6%), Los Angeles, California (13.5% vs 10.4%), and greater California (26.8% vs 23.8%) tumor registries. Moreover, the Detroit and California tumor registries contributed almost two-thirds of the MIRP vs less than half of the RRP cohort. In addition, men undergoing MIRP vs RRP more often lived in metropolitan vs nonmetropolitan areas (95.3% vs 91.2%; $P=.007$). While pathologic tumor grade was similar, men undergoing MIRP vs RRP were more likely to have organ-confined disease (68.3% vs 60.8%; $P<.001$).

Ten men (0.5%) vs 58 men (0.8%) died within 1 year of MIRP vs RRP surgery ($P=.17$), and the mortality rate did not differ through the remainder of our study (0.8 vs 0.9 per 100 person-years; $P=.72$). Patients were censored from analysis at the time of death, and median follow-up was 2.8 years (range, 1 day to 5 years). Unadjusted associations are presented in TABLE 2. Results are generally consistent with adjusted associations. In the propensity-adjusted analyses (TABLE 3), men undergoing MIRP vs RRP experienced shorter length of stay (median, 2.0 vs 3.0 days; OR, 0.67; 95% CI, 0.58-0.72), were less likely to receive heterologous transfusions (2.7% vs 20.8%; OR, 0.11; 95% CI, 0.06-0.17), and were at lower risk of postoperative respiratory complications (4.3% vs 6.6%; OR, 0.63; 95% CI, 0.46-0.87), miscellaneous surgical complications (4.3% vs 5.6%; OR, 0.75; 95% CI, 0.56-0.99), and anastomotic stricture (5.8% vs 14.0%; OR, 0.38; 95% CI, 0.28-0.52).

However, men undergoing MIRP vs RRP experienced more genitourinary complications (4.7% vs 2.1%; OR, 2.28; 95% CI, 1.61-3.22) and were more often diagnosed as having incontinence (15.9 vs 12.2 per 100 person-years; OR, 1.3; 95% CI, 1.05-1.61) and erectile dysfunction (26.8 vs 19.2 per 100 person-years; OR, 1.4; 95% CI, 1.14-1.72). The

Figure. Use of Minimally Invasive vs Open Retropubic Radical Prostatectomy for Men Diagnosed as Having Prostate Cancer in 2002-2005 and Undergoing Surgery in 2003-2007



No. of patients				
Minimally invasive	244	542	843	309
Retropubic	2394	2218	1881	406

Table 2. Unadjusted Outcomes by Surgical Approach

	MIRP	RRP	*P* Value
Length of stay, median (IQR)	2 (1-2)	3 (2-4)	<.001
Heterologous blood transfusion, No. (%)	49 (2.5)	1383 (20.1)	<.001
30-Day postoperative complications, No. (%)			
Overall	422 (21.9)	1606 (23.4)	.31
Cardiac	39 (2.0)	206 (3.0)	.03
Respiratory	80 (4.2)	465 (6.8)	<.001
Genitourinary	77 (4.0)	150 (2.2)	<.001
Wound	31 (1.6)	129 (1.9)	.41
Vascular	56 (2.9)	265 (3.9)	.08
Miscellaneous medical	181 (9.4)	598 (8.7)	.49
Miscellaneous surgical	91 (4.7)	387 (5.6)	.15
Death	2 (0.1)	12 (0.2)	.46
Anastomotic stricture, No. (%)[a]	99 (5.3)	946 (14.2)	<.001
Incontinence per 100 person-years[b]			
Diagnosis	18.2	11.9	<.001
Procedures	9.5	8.5	.30
Erectile dysfunction per 100 person-years[b]			
Diagnosis	33.8	18.2	<.001
Procedure	2.8	2.1	.04
Additional cancer therapy per 100 person-years			
Overall	6.1	6.9	.18
Radiation	4.3	4.9	.16
Hormone	3.5	3.7	.58
Death during the study period	0.7	0.9	.11

Abbreviations: IQR, interquartile range; MIRP, minimally invasive radical prostatectomy; RRP, open retropubic radical prostatectomy.
[a] Men who underwent surgery in 2007 were excluded because of insufficient follow-up to capture this outcome.
[b] Men who underwent surgery in the latter half of 2006 through the end of 2007 were excluded because of insufficient follow-up to capture this outcome.

need for additional cancer therapies was similar by surgical approach (8.2 vs 6.9 per 100 person-years; OR, 1.19; 95% CI, 0.84-1.69).

COMMENT

For many disease processes, minimally invasive surgery offers distinct, consistently reproducible advantages compared with open approaches, including shorter hospital stays, fewer inpatient procedures, and lower costs. However, RRP is performed through a relatively small incision that is infrequently associated with significant pain and has relatively short lengths of stay, averaging 1 to 3 days at high-volume referral centers.[34-36] Some studies suggest that MIRP vs RRP results in significantly less blood loss, lower transfusion rates, less use of postoperative analgesics, and quicker convalescence.[35,37-40] However, distinguishing perception from reality may be difficult for novel procedures such as MIRP,[39] particularly with assertions in the popular media of lower complication rates, shorter recovery time, better cancer removal, and faster removal of urinary catheter with robotic-assisted MIRP.[6]

Our study has several important findings. First, MIRP has been rapidly adopted since the initial suggestion of potential advantages over RRP.[3,4] Additionally, we observed significant sociodemographic and geographic variation in use of MIRP vs RRP. Black and Hispanic vs white and Asian men were less likely to undergo MIRP vs RRP. In addition, living in areas of higher socioeconomic status based on education and income was associated with greater receipt of MIRP vs RRP. This sociodemographic variation may result from the highly successful robotic-assisted MIRP marketing campaign[10] disseminated via the Internet,[41] radio, and print media channels[5,6] likely to be frequented by men of higher socioeconomic status. Additionally, black men and Hispanic men and men with lower socioeconomic status may not have access to networks or surgeons that offer MIRP.

Second, men undergoing MIRP vs RRP experienced shorter lengths of stay and were less likely to receive blood transfusions or develop postoperative respiratory and miscellaneous surgical complications. However, MIRP vs RRP was associated with an almost 2-fold increase in the odds of postoperative genitourinary complications.

Third, men undergoing MIRP vs RRP were more likely to be diagnosed as having incontinence and erectile dysfunction following surgery, even after adjusting for differences in baseline rates of these conditions. Because these outcomes were based on the presence of diagnosis codes only, it is not clear if men were more likely to have these conditions or were more likely to report them to a clinician. Men opting for MIRP may have heightened expectations for a heavily marketed "innovative" procedure, which may lead to greater dissatisfaction and regret compared with RRP.[42] Alternatively, this difference may be attributable to the lengthy learning curve[12] and relative changes in rates of MIRP vs RRP surgical technique during our study period. Nevertheless, we observed no difference in rates of procedures for incontinence or erectile dysfunction.

Fourth, after adjustment for patient and tumor characteristics, men undergoing MIRP vs RRP had similar rates of additional cancer therapy, a surro-

Table 3. Propensity Model–Adjusted Outcomes by Surgical Approach[a]

Outcomes	MIRP	RRP	MIRP vs RRP, Ratio (95% Confidence Interval)[b]	*P* Value
Length of stay, median (IQR)[c]	2 (1-2)	3 (2-4)	0.67 (0.58-0.72)	<.001
Heterologous blood transfusion, %	2.7	20.8	0.11 (0.06-0.17)	<.001
30-Day complications, %				
Overall	22.2	23.2	0.95 (0.77-1.16)	.58
Cardiac	2.4	2.9	0.81 (0.49-1.33)	.37
Respiratory	4.3	6.6	0.63 (0.46-0.87)	.004
Genitourinary	4.7	2.1	2.28 (1.61-3.22)	.001
Wound	2	1.9	1.05 (0.61-1.82)	.86
Vascular	3.4	3.9	0.86 (0.55-1.35)	.50
Miscellaneous medical	10	8.5	1.19 (0.89-1.6)	.26
Miscellaneous surgical	4.3	5.6	0.75 (0.56-0.99)	.03
Death	0.1	0.2	0.31 (0.07-1.28)	.05
Anastomotic stricture, %[d]	5.8	14.0	0.38 (0.28-0.52)	<.001
Incontinence per 100 person-years[e]				
Diagnosis	15.9	12.2	1.3 (1.05-1.61)	.02
Procedures	7.8	8.9	0.87 (0.69-1.1)	.24
Erectile dysfunction per 100 person-years[e]				
Diagnosis	26.8	19.2	1.40 (1.14-1.72)	.009
Procedure	2.3	2.2	1.05 (0.74-1.51)	.78
Additional cancer therapy per 100 person-years				
Overall	8.2	6.9	1.19 (0.84-1.69)	.35
Radiation	5.1	4.9	1.05 (0.84-1.32)	.67
Hormone	5.3	3.7	1.42 (0.88-2.32)	.21
Death during the study period per 100 person-years	0.8	0.9	0.91 (0.53-1.57)	.72

Abbreviations: IQR, interquartile range; MIRP, minimally invasive radical prostatectomy; RRP, open retropubic radical prostatectomy.

[a] The weighted propensity score adjusted for the following: year of surgery, age, comorbidity, baseline urinary incontinence, baseline erectile dysfunction, race/ethnicity, marital status, education, income, Surveillance, Epidemiology, and End Results region, population density, pathologic grade, and stage.

[b] The MIRP vs RRP ratios are median ratios for length of stay; odds ratios for heterologous transfusion, 30-day complications, and anastomotic stricture; and rate ratios for incontinence, erectile dysfunction, and additional cancer therapy.

[c] Length-of-stay odds ratio determined by the ratio of the medians.

[d] Men who underwent surgery in 2007 were excluded because of insufficient follow-up to capture this outcome, and the propensity score was recalculated for this outcome.

[e] Men who underwent surgery in the latter half of 2006 through the end of 2007 were excluded because of insufficient follow-up to capture this outcome, and the propensity score was recalculated for these outcomes.

gate for cancer control. In contrast with a recently published, population-based study that demonstrated greater risks of anastomotic stricture and worse cancer control with MIRP vs RRP[3], we observed a lower stricture rate and similar cancer control for MIRP vs RRP. Anastomotic strictures require additional surgery to dilate or incise the scar tissue under general anesthesia, which may result in incontinence, requiring placement of an artificial urinary sphincter in severe cases.[40,43] The different results may be related to differences in the study populations. The prior study examined a 5% random sample of Medicare beneficiaries nationwide[3] vs 100% of the Medicare beneficiaries in SEER registry areas in this study. This is particularly relevant because almost two-thirds of MIRPs in our study were performed in Detroit and California, regions containing high-volume MIRP centers,[5,44-46] where outcomes might be better.

Our findings must be interpreted within the context of limitations of our study design. First, claims files are primarily designed to provide billing information, not detailed clinical information. More comprehensive clinical data on severity of illness and comorbidity might have influenced the associations we identified. However, Medicare claims have a high degree of validity for detecting complications of prostatectomy, with 89% of Medicare complications corroborated by medical record abstraction.[47]

Second, short-term prostate cancer survival is high, and lengthier follow-up is needed to assess differences in cancer recurrence.

Third, our finding that men were more likely to be diagnosed as having urinary incontinence and erectile dysfunction following MIRP vs RRP is subject to observer bias. For instance, erectile dysfunction that impairs quality of life but does not necessitate seeking medical attention may not be captured from Medicare claims, and patient self-assessment with validated quality-of-life instruments provides a more precise measure of these outcomes. Moreover, we were unable to adjust for nerve-sparing surgical technique during radical prostatectomy, which improves postoperative sexual function.[48]

Fourth, MIRP included procedures performed with and without robotic assistance because both share a common CPT code. We were therefore unable to distinguish whether the robot was used during laparoscopy; however, the intraoperative strategy is similar and the prostatic anatomy is by definition identical.[49(p546, discussion)] Contemporary estimates of US robotic-assisted MIRP use range from 50% to 70%,[50-52] whereas a recent survey revealed a 25% to 75% decline in radical prostatectomy volume among urologists performing RRP and MIRP without robotic assistance.[53]

Fifth, this is an observational study of practice patterns and outcomes for elderly men undergoing surgery in SEER regions, and despite careful adjustment with propensity score methods, there may be unobserved differences in the groups for which we were unable to adjust. In addition, our findings may not be generalizable to younger men and those undergoing radical prostatectomy outside SEER regions, particularly because there is geographic variation in the use of MIRP and RRP that may result in variation in outcomes.[3,14,20,54]

CONCLUSION

During our study period, the use of MIRP increased, and men undergoing MIRP vs RRP experienced fewer transfusions, respiratory and miscellaneous surgical complications, and anastomotic strictures but more genitourinary complications and a greater likelihood of being diagnosed as having incontinence and erectile dysfunction in the long term. In light of the mixed outcomes associated with MIRP, our finding that men of higher socioeconomic status opted for a high-technology alternative despite insufficient data demonstrating superiority over an established gold standard may be a reflection of a society and health care system enamored with new technology that increased direct and indirect health care costs but had yet to uniformly realize marketed or potential benefits during early adoption.

Author Contributions: Dr Hu had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
Study concept and design: Hu, Lipsitz, Barry, D'Amico, Keating.
Analysis and interpretation of data: Hu, Gu, Lipsitz, D'Amico, Weinberg, Keating.
Drafting of the manuscript: Hu, Gu, Lipsitz, D'Amico, Weinberg.
Critical revision of the manuscript for important intellectual content: Hu, Gu, Lipsitz, Barry, D'Amico, Keating.
Statistical analysis: Gu, Lipsitz, Keating.
Administrative, technical, or material support: Weinberg.
Study supervision: Hu, Barry, D'Amico, Keating.
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Comparative Effectiveness of Perineal Versus Retropubic and Minimally Invasive Radical Prostatectomy

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Purpose: While perineal radical prostatectomy has been largely supplanted by retropubic and minimally invasive radical prostatectomy, it was the predominant surgical approach for prostate cancer for many years. In our population based study we compared the use and outcomes of perineal radical prostatectomy vs retropubic and minimally invasive radical prostatectomy.

Materials and Methods: We identified men diagnosed with prostate cancer from 2003 to 2005 who underwent perineal (452), minimally invasive (1,938) and retropubic (6,899) radical prostatectomy using Surveillance, Epidemiology and End Results-Medicare linked data through 2007. We compared postoperative 30-day and anastomotic stricture complications, incontinence and erectile dysfunction, and cancer therapy (hormonal therapy and/or radiotherapy).

Results: Perineal radical prostatectomy comprised 4.9% of radical prostatectomies during our study period and use decreased with time. On propensity score adjusted analysis men who underwent perineal vs retropubic radical prostatectomy had shorter hospitalization (median 2 vs 3 days, $p < 0.001$), received fewer heterologous transfusions (7.2% vs 20.8%, $p < 0.001$) and required less additional cancer therapy (4.9% vs 6.9%, $p = 0.020$). When comparing perineal vs minimally invasive radical prostatectomy men who underwent the former required more heterologous transfusions (7.2% vs 2.7%, $p = 0.018$) but experienced fewer miscellaneous medical complications (5.3% vs 10.0%, $p = 0.045$) and erectile dysfunction procedures (1.4 vs 2.3/100 person-years, $p = 0.008$). The mean and median expenditure for perineal radical prostatectomy in the first 6 months postoperatively was $1,500 less than for retropubic or minimally invasive radical prostatectomy ($p < 0.001$).

Conclusions: Men who undergo perineal vs retropubic and minimally invasive radical prostatectomy experienced favorable outcomes associated with lower expenditure. Urologists may be abandoning an underused but cost-effective surgical approach that compares favorably with its successors.

Key Words: prostate, prostatic neoplasms, prostatectomy, perineum, complications

Abbreviations and Acronyms

ED = erectile dysfunction

MIRP = minimally invasive RP

PLND = pelvic lymph node dissection

PRP = perineal RP

RP = radical prostatectomy

RRP = retropubic RP

SEER = Surveillance, Epidemiology and End Results

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After the first reported series of RP via a perineal approach in 1905, PRP became the standard prostate cancer surgical treatment for much of the 20th century.[1] Perineal incision proximity to the prostate, decreased blood loss, minimal pain, and ease of the approach in obese men and in those with prior abdominal surgery contributed to PRP being the predominant approach. PRP use decreased after the popularity of external beam radiation therapy in the 1970s and the description of nerve sparing RRP by

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Walsh et al in the 1980s, which obviated the need for a second incision for PLND.[2] However, after the advent of prostate specific antigen screening, resultant stage migration and increasing adoption of MIRP, the PLND rate during RP decreased.[3] Also, the indication for and benefit of PLND has been debated for low risk disease.[4] Given that PRP is associated with less postoperative pain and a shorter hospital stay than RRP, it was suggested that PRP may be underused in cases in which concurrent PLND is unnecessary.[5,6]

In the absence of randomized, controlled trials, population based studies of comparative effectiveness allow the evaluation of competing therapies across a broad range of providers in various health settings. We determined contemporary PRP use and outcomes compared to those of MIRP and RRP.

MATERIALS AND METHODS

Data

Our study was approved by the institutional review board. Participants were de-identified and the consent process was waived. We identified 137,217 men 65 years old or older who were diagnosed with prostate cancer from 2002 to 2005 and followed through December 31, 2007 using SEER-Medicare linked data.[7]

Study Exclusions

Excluded from analysis were 10,441 men enrolled in a health maintenance organization and/or those not enrolled in Medicare Parts A and B throughout the study duration since claims are not reliably submitted in these men. To increase sensitivity to detect postoperative radiation therapy we restricted analysis to men with prostate cancer diagnosed as the only cancer and excluded 4,628 with other cancers. This yielded a study cohort of 9,289 men who underwent RP during 2003 to 2007 based on CPT-4 codes, including 55840, 55842 and 55845 for RRP, 55866 for MIRP, and 55810, 55812 and 55815 for PRP. Other groups have used CPT-4 code 55899 (unspecified male genitourinary procedure) with a RRP CPT-4 code to ascertain MIRP but Medicare does not recognize this coding variant and it was excluded from analysis.

Outcomes

We examined mortality/morbidity, length of stay, anastomotic stricture, incontinence and ED diagnoses and procedures, and additional cancer therapy. Postoperative complications by category and transfusions were assessed within 30 days of surgery. Postoperative mortality was defined as death within 30 days of RP. We assessed anastomotic strictures 31 to 365 days after surgery. Incontinence and ED diagnoses and procedures were evaluated more than 18 months after surgery, which is the time required for urinary and sexual function recovery to plateau.[8] Finally, we identified men who underwent additional cancer therapy (radiation and/or hormonal treatment) after prostatectomy as a surrogate for cancer control.[9]

Expenditures

To best attribute the costs associated with competing surgical approaches we assessed Medicare payments for 6 months including and after RP as 1) total Medicare reimbursements and 2) prostate cancer related Medicare reimbursements for claims submitted with a prostate cancer diagnosis code (ICD-9 185.0).

Control Variables

Patient age was obtained from the Medicare file. The SEER registry provided data on race/ethnicity, census measurements of median household income and the proportion of individuals with at least a high school education, SEER region, population density and marital status. Due to small numbers we combined the New Mexico, rural Georgia and Atlanta SEER registries. Comorbidity using the Klabunde modification of the Charlson index, and preoperative diagnoses of incontinence and ED were based on inpatient, outpatient and carrier claims during the year before surgery.[10] Finally, we adjusted for year of surgery since outcomes may have improved with time.

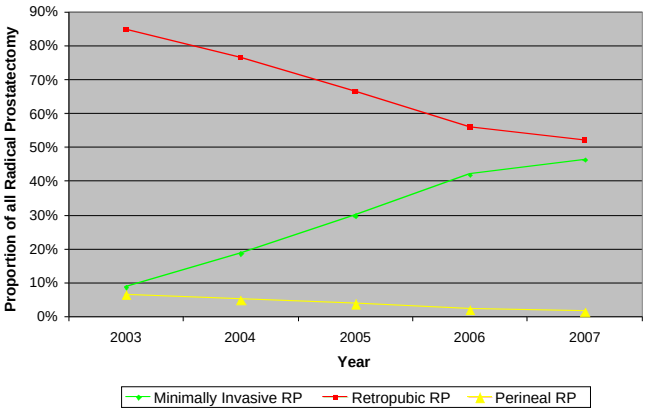
Statistical Analysis

PRP, RRP and MIRP annual use rates were derived and temporal trends in use were compared with the Mantel-Haenszel chi-square test for trend, adjusted for surgeon clustering. For dichotomous outcomes occurring within a fixed interval, such as 30 and 31 to 365-day (anastomotic stricture) outcomes, we compared proportions (the number of events divided by the number of patients) for PRP vs MIRP and RRP. We compared rates for outcome variables without an upper time bound for which followup could vary.[11] We also compared median length of stay among the groups.

Since men who underwent PRP differed from those who underwent MIRP and RRP in terms of demographic characteristics, we used weighted propensity score methods to adjust for these differences.[12,13] Propensity score methods control for all observed confounding factors that may influence group assignment and outcome using a single composite measure. They also balance patient characteristics between groups, as would occur in a randomized experiment.

To perform propensity score adjustment we used a logistic regression model to calculate the probability of undergoing PRP vs MIRP and RRP based on all covariates described, and then weighted data on each patient based on the inverse propensity of being in 1 of the 2 treatment groups.[14] Covariate balance was assessed after adjustment. We used generalized estimating equations to account for surgeon clustering on weighted propensity adjusted analysis. To compare proportions we fit generalized estimating equation logistic regressions with surgical approach (PRP vs MIRP and RRP) as the only covariate, weighted by the inverse propensity score. All tests were considered statistically significant at $\alpha = 0.05$. All analysis was done with SAS®, version 9.1.3.

Due to confidentiality, values less than 11 may not be reported directly or in a derivable way for any SEER-Medicare data obtained from the National Cancer Institute. Therefore, for any patient group with fewer than 11 patients, data are shown as less than 2.4% in the PRP



RP rate by approach during study period

group, less than 0.6% in the MIRP group and less than 0.2% in the RRP group.

RESULTS

From 2003 to 2007 in the study cohort 6,899 men underwent RRP, 1,938 underwent MIRP and 452 underwent PRP. During the study period we found increased use of MIRP with a corresponding decrease in the rate of RRP and PRP (see figure). PRP use decreased more than 3-fold during the study period. Less than 2% of RPs were done via a perineal approach in 2007 vs 6.5% in 2003.

We noted multiple demographic differences in PRP vs MIRP and RRP. Men undergoing PRP vs MIRP were more likely to have comorbidities ($p = 0.008$). Men with lower education and median income were more likely to undergo PRP than MIRP ($p = 0.028$ and <0.001, respectively). Men undergoing PRP vs MIRP were more likely to reside in a nonmetropolitan area ($p < 0.001$). PRP was more commonly done in the South and Midwest compared to MIRP and RRP ($p = 0.014$ and 0.004, respectively). Baseline incontinence was lower for PRP vs MIRP and RRP ($p < 0.001$ and 0.040, respectively). While baseline ED was lower for PRP vs MIRP ($p < 0.001$), there were no differences compared to RRP. We also noted no differences in age, race, marital status, or tumor grade or stage by surgical approach.

When comparing unadjusted outcomes, men undergoing PRP vs RRP had shorter length of stay (2 vs 3 days, $p < 0.001$), and were less likely to undergo blood transfusion (7.1% vs 20.1%, $p < 0.001$) and have anastomotic stricture (8.2% vs 14.2%, $p = 0.002$). The overall 30-day complication rate was lower in men undergoing PRP vs RRP (16.7% vs 23.4%, $p = 0.002$). However, additional cancer therapy did not differ for PRP vs RRP (5.8% vs 6.9%, $p = 0.147$). When we compared unadjusted outcomes in the PRP and MIRP cohorts, men undergoing PRP vs MIRP were more likely to undergo blood transfusion (7.1% vs 2.5%, $p < 0.001$). However, the 30-day complication rate was higher in the MIRP group (16.7% vs 21.9%, $p = 0.016$) while anastomotic stricture rate was higher in the PRP cohort (8.2% vs 5.3%, $p = 0.048$). Finally, PRP had the lowest mean and median Medicare expenditures, followed by RRP and MIRP (see table).

On propensity score adjusted analysis PRP vs RRP was associated with fewer blood transfusions (7.2% vs 20.8%, $p < 0.001$) and shorter length of stay (median 2 vs 3 days, $p < 0.001$). The additional cancer therapy incidence (radiation and hormonal) was higher in the RRP group (4.9% vs 6.9%, $p = 0.020$). There were no differences in PRP vs RRP 30-day complications, mortality, postoperative stricture, or ED or incontinence diagnosis and treatment. When comparing outcomes between PRP and MIRP, PRP was associated with more blood transfusions (7.2% vs 2.7%, $p = 0.018$), fewer miscellaneous medical complications (5.3% vs 10.0%, $p = 0.045$) and fewer procedures for ED (1.4 vs 2.3/100 person-years, $p = 0.008$). MIRP and PRP did not differ in length of stay, overall 30-day complications, mortality, incontinence diagnosis or procedures and additional cancer therapy.

DISCUSSION

RP gained popularity through the mid 1900s with a demonstrated survival benefit for prostate cancer.[15] In the 1970s an evolution from the perineal to the retropubic approach occurred due to the loss of familiarity with perineal surgical anatomy as simple open perineal prostatectomy was abandoned, familiarity with retropubic anatomy as simple retropubic open prostatectomy and radical cystectomy became more common, and increased interest in PLND and the lack of the need for a second incision to perform lymphadenectomy (P. Walsh, personal communication, November 16, 2009). However, with the subse-

Medicare payments within 6 months of RP by surgical approach

	No. Pts	Mean/Median Payment* ($)
Overall:		
PRP	381	11,953/11,019
MIRP	1,548	14,939/13,335
RRP	5,565	14,301/12,767
Prostate Ca (ICD-9 185.0):		
PRP	381	9,957/9,339
MIRP	1,548	12,289/11,324
RRP	5,565	11,884/10,853

* $p < 0.001$.

quent use of prostate specific antigen for prostate cancer screening in the 1990s and corresponding stage migration, the incidence of positive lymph nodes at RP has decreased to less than 3%.[16] Given the low rate of lymph node involvement, the need for concurrent PLND during RP remains debatable. Also, prior groups noted that PRP has shorter operative time and decreased intraoperative operative cost than MIRP or RRP,[17] although the increased surgical expense may be offset by significantly lower nonoperative hospital costs. This was the finding in a retrospective review of 452 patients treated for clinically localized prostate cancer in which total hospital cost differences were less for minimally invasive approaches (robot assisted MIRP and cryosurgical ablation of the prostate) than in the open (PRP or RRP) surgery groups.[18] However, these studies did not account for delayed costs, such as treatment for ED or urinary incontinence, salvage therapy and associated time lost at work. Additional analysis is needed to completely capture these associated costs.

We performed a population based analysis comparing PRP vs RRP and MIRP outcomes with several important findings. 1) We found a significant increase in the rate of MIRP use with concomitant cannibalization of RRP and PRP. During the study period PRP decreased from 6.5% to less than 2% of all RPs done in this cohort. As the scientific literature balances reports of costs and mixed outcomes of MIRP,[17–20] competing approaches to RP may come under greater scrutiny by payors, patients and physicians. This decreased use limits PRP training and exposure of this approach to the next generation of urologists. A survey of recent urology residents revealed that only 13% of those not exposed to PRP used the procedure in practice.[20]

2) Men undergoing MIRP vs PRP were more likely to come from areas of higher socioeconomic status and from metropolitan areas. This difference may be due to the successful marketing approach of robot-assisted MIRP through print media and the Internet as well as early adoption of the robot at wealthier centers.[11]

3) When we compared men undergoing PRP vs RRP, PRP was associated with shorter length of stay and fewer heterologous blood transfusions. While there was no difference in the postoperative stricture rate between PRP and RRP, PRP was associated with less adjuvant therapy use. While this may reflect improved cancer control after PRP, it may also reflect differences in lymph node sampling since adjuvant therapy may be initiated with node positive disease that remains undiagnosed by PRP alone. PRP was associated with lower cost due to decreased median hospital stay, blood transfusion and adjuvant therapy use, consistent with a single institution comparison.[18] Also, total Medicare payments within 6 months of surgery were lower for PRP than for RRP or MIRP with a mean and median PRP expenditure greater than $1,500 less than that for RRP or MIRP. While this may not capture all payments associated with long-term complications beyond 6 months postoperatively, it captures the associated expense of rehospitalizations, emergency department visits and additional radiological or surgical procedures.

4) Comparison between men undergoing PRP vs MIRP revealed no difference in length of stay, although PRP was associated with a 3-fold increase in the likelihood of heterologous blood transfusion. However, this increased PRP blood transfusion rate was not offset by any MIRP advantages in short-term or intermediate term outcomes. MIRP was associated with an almost 2-fold higher rate of medical complications within 30 days of surgery compared with PRP. Cancer control and stricture rates did not differ significantly for PRP vs MIRP.

5) PRP vs MIRP was associated with fewer procedures for ED but we did not account for surgeon skill and experience. For instance, PRP surgeons who have not changed to newer approaches may be comfortable with their PRP ability due to greater experience and proficiency, resulting in better outcomes.

Our findings must be interpreted in the context of the study design. 1) Our study was restricted to Medicare beneficiaries older than 65 years who resided in SEER regions. Thus, these results may not be applicable to younger men or those undergoing surgery outside SEER regions due to geographic variation in RP use and outcomes.[21] 2) We could not distinguish between MIRP with and without robotic assistance since the 2 procedures share a common CPT-4 code. However, robotic assisted MIRP use surged from 1% of RPs in 2001 to 40% in 2006,[22,23] with a current estimate of 50% to 70%.[24] Concurrently MIRP without robotic assistance is disappearing in the United States, consistent with a recent survey of urologists showing a 25% to 75% decrease in surgical volume among those using a nonrobotic approach to RP.[25,26] 3) Observer bias may have a role in the diagnosis of ED and urinary continence, as captured by Medicare claims data. Men diagnosed with these conditions were sufficiently bothered to bring it to the attention of physicians who entered the diagnosis. Patient self-report using validated quality of life instruments remains the gold standard to assess these outcomes. 4) As in any adjusted analysis, propensity score methods cannot control for unmeasured confounders and have other limitations.[27]

CONCLUSIONS

Despite decreased use, PRP has outcomes that are equivalent or improved compared to those of RRP and MIRP with lower cost within the first 6 months postoperatively. Since there is increased attention on comparative effectiveness analysis due to increasing health care costs, our findings contribute to other studies showing that PRP is a favorable and perhaps prematurely abandoned alternative to RP.

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Oncology

Determinants of Performing Radical Prostatectomy Pelvic Lymph Node Dissection and the Number of Lymph Nodes Removed in Elderly Men

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OBJECTIVE Controversy persists regarding the adequacy of pelvic lymph node dissection (PLND) and cancer control when comparing minimally invasive radical prostatectomy (MIRP) and open radical prostatectomy (RRP). We characterized determinants of performance and extent of PLND during radical prostatectomy in elderly men.

METHODS A population-based study was conducted comprised of 5448 men ≥65 years undergoing RRP and MIRP during 2004 to 2006 from Surveillance, Epidemiology, and End Results (SEER)–Medicare-linked data. Multivariable logistic regression was used to assess the effect of demographic and tumor characteristics, surgical approach, and surgeon volume on the likelihood of performing PLND.

RESULTS PLND was performed for 87.6% vs. 38.3% of men undergoing RRP vs. MIRP ($P < .001$). Among RRP, 82.6% vs. 4.6% underwent extended vs. limited PLND, with a median yield of 4 vs. 3 lymph nodes ($P < .001$). Median MIRP PLND yield was 3 lymph nodes. In adjusted analyses, men undergoing RRP vs. MIRP (odds ratio [OR] 16.7; 95% confidence interval [CI], 11.1-25.0), those with few vs. multiple comorbidities (OR 1.4, 95% CI 1.02-1.91), intermediate (OR 1.87; 95% CI 1.48-2.37), and high (OR 2.77; 95% CI 2.02-3.78) vs. low-risk features, and men treated by high-volume surgeons (OR 1.008; 95% CI 1.004-1.011) were more likely to undergo PLND. Conversely, Hispanic (OR 0.68, 95% CI 0.49-0.96) vs. white men were less likely to undergo PLND.

CONCLUSIONS Independent of tumor characteristics, men undergoing RRP vs. MIRP were more likely to undergo PLND with greater lymph node yield and racial variation observed. Further studies are needed to determine the appropriate use of PLND. UROLOGY xx: xxx, xxxx. © 2010 Elsevier Inc.

As surgical evolution unfolds with a shift from open radical prostatectomy (RRP) to minimally invasive radical prostatectomy (MIRP), debates persist regarding the adequacy of pelvic lymph node dissection (PLND) and cancer control. The promise of imaging techniques for accurate staging remains unfulfilled, and PLND remains the most accurate and reliable staging method for detecting occult prostate cancer metastases.[1] Moreover, with greater enthusiasm for extended versus limited PLND, unanswered questions linger concerning the adequacy of PLND during MIRP vs. RRP.

The incidence of lymph node metastases has plummeted from the 40% to 20% range[2,3] before prostate-specific antigen (PSA) screening and resultant stage migration to current levels of 1.2%, with limited and 3.3% to 6.5% with extended PLND at high-volume referral centers.[4,5] Moreover, there is considerable guideline variation concerning indications and anatomic extent of PLND: (1) PLND, extent unspecified, for high risk disease[6]; (2) extended PLND for those with ≥7% predicted risk of involvement[7]; or (3) extended PLND for intermediate- and high-risk disease features.[8] In addition, there is considerable practice pattern variation by surgical approach, because a recent nationwide study demonstrated significant disparity in the use of PLND in 83% of RRP vs. only 17% of MIRP,[9] although the study design precluded assessment of the influence of tumor characteristics on PLND used. Finally, extended PLND has been associated with an increased risk of complications[5] and longer hospital stays, and therefore carry the potential of increased morbidity and costs.[10]

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The purpose of our population-based study was to: (1) determine clinical and pathologic characteristics associated with performing PLND during RP; and (2) assess the variation in yield and morbidity of PLND by surgical approach, surgeon volume, and extent of dissection.

SUBJECTS AND METHODS

Data

We used Surveillance, Epidemiology, and End Results (SEER)–Medicare data, which is a collaborative effort[11] between the U.S. National Cancer Institute (NCI), which collects population-based cancer registry data from 16 SEER areas covering approximately 26% of the U.S. population with Medicare administrative data from the Center for Medicare and Medicaid Services (CMS). Medicare serves as the primary payer of health insurance for elderly Americans, and surgeons must use *Current Procedural Terminology Coding System*, 4th edition (CPT-4) codes to designate medical procedures to be reimbursed.

Study Cohort

We identified men aged ≥65 years diagnosed with prostate cancer from 2004 to 2005 undergoing radical prostatectomy from 2004 to 2006 (n = 5448) using CPT-4 55840, 55842, and 55845 for RRP without, with limited, and with extended PLND; 55866 for MIRP alone; and 55866 and 38571 for MIRP with PLND. The dependent variable of our analysis was concurrent PLND with radical prostatectomy. Although CPT-4 code 38770 may be used to capture open PLND, it failed to yield additional subjects who underwent PLND at the time of prostatectomy. Moreover, we excluded perineal radical prostatectomy, because it accounted for <5% of all radical prostatectomies performed during our study period. Finally, CPT-4 code 55899 (unspecified male genitourinary procedure) may be used to specify MIRP with robotic assistance for private health plans,[12] but Medicare does not recognize this coding schema and it was therefore excluded. Finally, we excluded men not fully enrolled in Medicare or simultaneously enrolled in health maintenance organizations (because their claims are not reliably submitted).

Study Variables

Age was obtained from the Medicare file; race, census-tracked measures of median household income and proportion of individuals with at least a high school education, SEER region, population density (urban vs. rural), marital status, and tumor characteristics were obtained from the SEER registry data (Table 1). Comorbidity was assessed using the Klabunde modification of the Charlson index during the year before surgery.[13] SEER regions were grouped as Northeast, Midwest, South, and West, consistent with the U.S. Census. In addition, PSA, Gleason grade, and clinical stage were used to stratify men according to the D'Amico risk criteria.[14]

We determined surgeon volume for each type of procedure by aggregating the number of procedures performed from 2004 to 2006. Although assessing surgeon volume as a categorical variable allows for more intuitive clinical interpretability and comparisons, surgeon experience is acquired one case at a time. Therefore, we assessed surgeon volume both categorically and continuously. Initially, we analyzed MIRP and RRP surgeon volume categorically as quartiles. However, this classification resulted in <10 MIRP surgeons in the highest-volume category and the NCI precludes the reporting of small cell sizes because of confidentiality concerns. We therefore re-stratified into tertiles, resulting in 11 MIRP and 81 RRP surgeons in the high-volume groups. Classifying surgeon volume into tertiles vs. quartiles did not alter the direction or significance of our findings.

Statistical Analysis

Unadjusted analysis was performed to compare demographic and tumor characteristics and surgeon volume using the Pearson χ^2 statistic, adjusting for clustering by surgeon. Adjusted analysis with logistic regression was performed to determine the likelihood of performing PLND while controlling for the potential confounder of surgeon volume as a continuous variable, surgical approach, risk stratification, age, comorbidities, race, and region. All tests were considered statistically significant at $\alpha = 0.05$. All analyses were performed with SAS version 9.1.3 (SAS Institute, Cary, NC).

RESULTS

The demographics of our study population are shown in Table 1. Wealthier men (P = .023) and those living in urban vs. rural areas (P = .032) were less likely to undergo PLND. There was a trend for men with fewer comorbidities to be more likely to undergo PLND (P = .056). Men with higher PSA, Gleason grade, and clinical stage were more likely to undergo PLND (P <.001, respectively). Accordingly, 998 (65.6%) of men with low-, 1761 (75.8%) of men with intermediate-, and 1064 (82.1%) of men with high-risk disease underwent PLND (P <.001).

When stratified by surgical approach (Table 2), PLND was performed more frequently with RRP vs. MIRP (87.6% vs. 38.3%, P <.001). Moreover, PLND was performed more frequently by high-volume MIRP and RRP surgeons (P <.001). Although there was less variation in using PLND between high- vs. low-volume RRP surgeons (88.4% vs. 84.9%), high- vs. low-volume MIRP surgeons were almost twice more likely to perform PLND (55.0% vs. 23.2%). In addition, one more lymph node was removed with RRP vs. MIRP (median 4 vs. 3, P <.001), with a trend toward a higher positive lymph node rate (2.5% vs. <1.5%, P = .057).

Among men undergoing RRP, 82.6% vs. 4.6% underwent an extended vs. limited PLND with a median of 4 vs. 3 lymph nodes removed (P = .032). We also examined complications attributable to PLND, such as lymphoceles, obturator nerve injury, and ureteral injury; however, these were uncommon events (<1%, respectively) and did not differ by surgical approach or by extent of PLND (limited vs. extended) during RRP. Furthermore, length of stay was 2 days for RRP and 3 days for MIRP and did not vary based on extent and performance of PLND.

In adjusted analysis (Table 3), men undergoing RRP vs. MIRP had 16 times greater odds of undergoing PLND (odds ratio [OR] 16.7, 95% confidence interval [CI] 11.1-25.0). Greater surgeon volume was associated with per-

Table 1. Demographic and tumor characteristics stratified by use of PLND

	No PLND (n = 1415)		PLND (n = 4033)		
Variable	n	%	n	%	*P* Value*
Year of surgery					
2004	455	32.2	1716	42.6	<.001
2005	759	53.6	1903	47.2	
2006	201	14.2	414	10.3	
Age (years)					
65-69	881	62.3	2498	61.9	.230
70-74	449	31.7	1237	30.7	
75+	85	6.0	298	7.4	
Charlson index					
0	999	70.6	2762	68.5	.056
1	315	22.3	1021	25.3	
2+	101	7.1	250	6.2	
Race					
White	1122	79.3	3220	79.8	.99
Black	100	7.1	293	7.3	
Hispanic	114	8.1	307	7.6	
Asian	60	4.2	164	4.1	
Marital status					
Not married	208	14.7	587	14.6	.179
Married	1105	78.1	3233	80.2	
Unknown	102	7.2	213	5.3	
% Of men with at least a high school education					
<75	256	18.1	751	18.6	.191
75-84.99	255	18.0	774	19.2	
85-89.99	246	17.4	802	19.9	
90+	657	46.5	1706	42.3	
Median income (USD)					
<35,000	335	23.7	1151	28.5	.023
35,000-44,999	313	22.1	935	23.2	
45,000-59,999	376	26.6	987	24.5	
≥60,000	390	27.6	960	23.8	
Region					
Northeast	180	12.7	433	10.7	.510
South	177	12.5	611	15.2	
Midwest	221	15.6	506	12.6	
West	837	59.2	2483	61.6	
Location					
Urban	1334	94.3	3694	91.6	.032
Rural	81	5.7	339	8.4	
PSA					
≤4	208	14.7	515	12.8	<.001
4.1-10	887	62.7	2294	56.9	
10.1-20	106	7.5	534	13.2	
>20	37	2.6	230	5.7	
Unknown	177	12.5	460	11.4	
Gleason score					
≤6	671	47.4	1407	34.9	<.001
7	616	43.5	1991	49.4	
8	73	5.2	348	8.6	
9/10†	34	2.4	251	6.2	
Clinical stage					
T1	791	55.9	1982	49.1	.006
T2	215	15.2	738	18.3	
T3+T4	16	1.1	83	2.1	
Unknown	393	27.8	1230	30.5	
D'Amico risk					
Low	524	37.0	998	24.8	<.001
Intermediate	563	39.8	1761	43.7	
High	232	16.4	1064	26.4	
Unknown	96	6.8	210	5.2	

* *P* values adjusted for clustering.
† Gleason 9 and 10 scores combined in compliance with NCI confidentiality policy.

Table 2. Use and yield of pelvic lymph node dissection by surgical approach and surgeon volume

	MIRP		RRP		
	n	%	n	%	*P* Value
PLND performed	573	38.3	3460	87.6	<.001
Surgeon volume					
Low	118	23.2	1133	84.9	<.001
Medium	174	36.4	1238	89.5	
High	281	55.0	1089	88.4	
Number of LN removed					
1-3	211	36.8	1030	29.8	.005
4-7	182	31.7	915	26.5	
≥7	68	11.9	836	24.2	
Unknown	112	19.5	679	19.5	
Median LN removed	3		4		<.001

LN = lymph node.

Table 3. Logistic regression model for use of pelvic lymph node dissection

Variable	OR	95% CI	*P* Value
Age (referent = 75+)			
65-69	0.92	0.68-1.24	.569
70-74	0.88	0.64-1.22	.446
Charlson Index (referent = 2+)			
0	1.3	0.99-1.7	.061
1	1.4	1.02-1.91	.038
Race (referent = White)			
Black	0.8	0.47-1.34	.393
Hispanic	0.68	0.49-0.96	.026
Asian	1.38	0.77-2.46	.275
D'Amico risk (referent = low)			
intermediate	1.83	1.44-2.32	<.001
High	2.57	1.94-3.4	<.001
Region (referent = West)			
Northeast	1.18	0.77-1.82	.438
South	1.23	0.69-2.22	.483
Midwest	1.12	0.58-2.16	.743
Surgical approach (referent = MIRP)			
RRP	16.7	11.1-25.0	<.001
Surgeon volume (continuous)	1.008	1.004-1.011	<.001

forming PLND (OR 1.008, 95% CI 1.004-1.011). In addition, intermediate- (OR 1.9, 95% CI 1.48-2.37) and high- (OR 2.77, 95% CI 2.02-3.78) vs. low-risk features increased the odds of performing PLND by almost 2- and 3-fold. Moreover, men with few (OR 1.40, 95% CI 1.02-1.91) vs. multiple comorbidities were more likely to undergo PLND. Finally, Hispanic vs. white men were less likely to undergo PLND (OR 0.68, 95% CI 0.49-0.96).

DISCUSSION

Indication and appropriate extent of PLND during radical prostatectomy remains controversial. Although PLND improves staging, prostate cancer metastasizes unpredictably, and PSA criteria are used to define recurrence and initiate adjuvant therapies in contrast to other malignancies that require surveillance imaging and lack a tumor marker. Allaf *et al.* suggested that extended vs. limited PLND leads to better cancer control.[4] Although extended vs. limited PLND were designated during 83.2% vs. 4.9% of RRP, it yielded only 1 additional lymph node on average (mean yield of 5.9 vs. 4.6 lymph nodes) in contrast to referral center yields of 11.6 vs. 8.9 nodes for extended vs. limited PLND.[4] Medicare reimbursed an additional $292 and $92, respectively, for extended and limited PLND vs. RRP alone,[15] and our population-based findings suggest that financial incentives may be driving practice patterns. Although less than a quarter of men presented with high-risk disease, almost three quarters underwent PLND, and positive lymph nodes were identified in <2% of the study population.

Our study has additional important findings. First, use of PLND was significantly greater during RRP vs. MIRP. This difference likely reflects greater surgeon inexperience with MIRP, because of the more recent dissemination, vs. RRP. Although MIRP PLND was used for 25% vs. 43% of men with low- vs. intermediate-risk disease, RRP PLND was used for 83% vs. 89% of men with low- vs. intermediate-risk disease. This suggests that PLND was overused for low- and intermediate-risk disease compared with certain guidelines.[6,7] However, men with high- and intermediate- vs. low-risk disease had greater odds of undergoing PLND. Although some have reported similar lymph node yields for RRP and MIRP,[16] others report higher lymph node yield with RRP vs. MIRP,[17] consistent with our population-based findings of 1 more lymph node removed with RRP vs. MIRP PLND.

Second, greater surgeon volume was associated with greater likelihood for performing PLND independent of surgical approach and tumor characteristics. This finding likely reflects inexperienced surgeons either forgoing PLND, because of increased risk of complications or prolonged operative times. Moreover, men with few vs. multiple comorbidities were more likely to undergo PLND, likely because of lower surgeon-perceived risk for complications in healthier men.[9]

Third, the risk of PLND-associated complications, such as obturator nerve and ureteral injury and lymphoceles, did not vary by surgical approach or extent of PLND during RRP. In contrast, others have reported higher complications and longer hospitalizations with extended vs. limited PLND.[5,10] However, there were greater differences in lymph node yields for extended vs. limited RRP PLND, indicating more aggressive extended PLND templates at these referral centers compared with our population-based difference of 1 lymph node between extended vs. limited RRP PLND. Therefore, similar yields from limited vs. extended RRP PLND in our study likely resulted from similar dissection templates and re-

sultant complications, despite differences in billing designation and Medicare reimbursement. Moreover, despite descriptions of lymph node dissection templates,[4,18] there is tremendous heterogeneity of radical prostatectomy surgical technique, and our population-based findings accentuate the need to reconcile PLND operative yield with billing designation.

Finally, Hispanic vs. white men were less likely to undergo PLND; however, disparity in PLND use was not observed for other races. Similarly, Hispanic vs. white and black men are less likely to undergo definitive therapy for prostate,[19] and the lower use of PLND among Hispanics may stem from patient rather than physician preferences. Conversely, racial differences in access to procedures, such as percutaneous transluminal coronary angioplasty and coronary artery bypass grafting have been observed for Hispanics.[20] However, our observational study does not allow us to determine whether PLND disparity for Hispanics stems from patient preference vs. limited access imposed by providers.

Our findings must be interpreted in the context of our study design. First, our study was limited to Medicare beneficiaries aged ≥65 years in SEER regions. Therefore, our results may not be generalizable to younger men or those undergoing surgery outside SEER regions. Second, we were unable to differentiate MIRP with vs. without robotic assistance because both share a common CPT-4 code. However, a recent survey revealed a 25% to 75% decline in surgeon volume among urologists using MIRP without robotic assistance.[21] Third, although SEER tumor registry provided tumor characteristics, the number of lymph nodes removed was not recorded for 19.5% of our study cohort. Finally, variation in specimen submission and pathologic interpretation may influence our findings. However, this also limits comparisons and generalizations between single-center studies.

CONCLUSIONS

Independent of tumor characteristics, elderly men undergoing RRP vs. MIRP were more likely to undergo PLND, with greater lymph node yield and racial variation observed. Further studies are needed to determine the appropriate use of PLND for elderly men with prostate cancer.

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BJUI BJU INTERNATIONAL

Population-based determinants of radical prostatectomy surgical margin positivity

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Level of Evidence 2b

OBJECTIVES

To characterize factors associated with positive surgical margins (PSMs) and derive population-based PSM cutoffs to evaluate surgeon performance in radical prostatectomy (RP).

METHODS

SEER-Medicare data were used to identify 4247 men diagnosed with prostate cancer during 2004–2005 who underwent RP up to 2006. We performed logistic regression to assess the impact of tumour characteristics, surgeon volume and surgical approach on the likelihood of PSMs for pT2 and PT3a disease. Moreover, we derived 25th and 10th percentile cutoffs from binomial distribution equations.

RESULTS

Overall, 19.4% of men experienced PSMs with a pT2 vs pT3a PSM rate of 14.9% vs 42% ($P < 0.001$). Extrapolating from our population-based results, a surgeon incurring more than three PSMs in 10 cases of pT2 disease performed below the 25th percentile. There was a trend for fewer PSMs with minimally invasive vs open RP (17.4% vs 20.1%, $P = 0.086$), and the PSM rate also decreased over the study period from 21.3% in 2004 to 16.6% in 2006 ($P = 0.028$) with significant geographic variation ($P < 0.001$). In adjusted analyses, temporal and geographic variation in PSM persisted, and men with high (odds ratio 3.68, 95% CI 2.82–4.81) and intermediate (odds ratio 2.52, 95% CI 2.03–3.13) vs low-risk disease were at greater odds to experience PSMs. Notably, neither surgical approach nor surgeon volume was significantly associated with PSMs.

CONCLUSION

Our population-based PSM benchmarks allow identification of under-performing outliers who may seek courses or video self-study to improve outcomes. There was significant temporal and geographic variation in PSMs but neither surgeon volume nor surgical approach was associated with PSMs.

KEYWORDS

positive margins, prostatectomy, minimally invasive, surgeon volume, outcomes

INTRODUCTION

Positive surgical margin status is a significant predictor of biochemical recurrence after radical prostatectomy [1]. Although positive surgical margins and greater PSA velocity, tumour grade and stage are associated with an increased risk of prostate cancer recurrence, only surgical margin status is influenced by surgical technique. In addition, positive surgical margins for organ-confined prostate cancer may serve as a quality indicator, and recent level 1 evidence shows a survival advantage when adjuvant radiotherapy is administered to counter this undesirable outcome [2,3]. Consequently, positive surgical margins increase the cost of treating prostate cancer secondary to the use of adjuvant radiotherapy and treatment of cancer recurrence.

Minimally invasive radical prostatectomy with and without robotic assistance has been rapidly adopted [4] but there are few comparisons of surgical margin status in minimally invasive surgery with that in open retropubic radical prostatectomy aside from single-centre studies [5]. Furthermore, some contend that the sense of palpation during retropubic radical prostatectomy, which is lacking with the minimally invasive approach, allows better assessment of the extent of tumour [6], potentially resulting in fewer positive margins and better cancer control. Our study objectives were: to characterize determinants of positive surgical margins and to derive population-based positive surgical margin benchmarks for surgeon self-assessment.

METHODS

Surveillance, Epidemiology, and End Results (SEER)–Medicare data were used for analyses, which comprise a linkage of population-based cancer registry data from 16 SEER areas covering approximately 26% of the US population with Medicare administrative data. The Medicare programme provides benefits to most Americans aged ≥65 years.

We identified 6153 men aged ≥65 years enrolled in Medicare Parts A and B, not

enrolled in the Medicare health maintenance organization (because their claims were not reliably submitted), diagnosed with prostate cancer in 2004 and 2005 who underwent open and minimally invasive radical prostatectomy from 2004 to 2006. We stratified the surgical approach on the basis of the Physicians Current Procedural Terminology Coding System 4th edition, (CPT-4): 55840, 55842, 55845 for open retropubic radical prostatectomy; and 55866 for minimally invasive radical prostatectomy [4,7]. Because SEER only captures positive margin characteristics for the American Joint Commission on Cancer pathological T2 and T3a disease, we excluded 293 men with pathological stage T3b, 63 men with pathological T4 and 1132 men with missing pathological information. We also excluded 318 men who underwent radical prostatectomy outside SEER regions to avoid misclassification of surgeon volume.

The control variables were obtained as follows. Patient age was obtained from the Medicare file; race, census tract measures of median household income and high school education, Census region, population density (urban vs rural), and marital status were obtained from SEER registry data. Comorbidity was assessed using the Klabunde modification of the Charlson index during the year before surgery [8]. Variables were categorized as in Table 1. Additionally, we used PSA, Gleason Grade and stage to stratify men to low-risk, intermediate-risk and high-risk disease [9]. However, clinical tumour stage was missing/unknown for almost one-third of our subjects. Moreover, there was a lower than expected percentage of men (18%) in the low-risk group compared with a community cohort [10]. We hypothesized that biopsy findings, rather than indication for biopsy, may have to be used for clinical staging, contrary to American Joint Committee on Cancer guidelines. We therefore used a modified D'Amico risk stratification that omitted clinical stage, resulting in a low-risk designation for 29% of our cohort.

Because surgeon rather than hospital volume is the more significant determinant of outcomes after retropubic radical prostatectomy [11], we determined surgeon volume by aggregating the number of procedures performed from 2004 to 2006. We assessed surgeon volume a priori as both a continuous and a categorical variable.

TABLE 1 Demographics of the study population

Characteristic	Categories	Total	Positive margin, *n* (%)	*P*-value
Year of surgery	2004	1779	378 (21.3)	0.028
	2005	2058	376 (18.3)	
	2006	410	68 (16.6)	
Age (years)	65–69	2620	485 (18.5)	0.203
	70–74	1332	270 (20.3)	
	≥75	295	67 (22.7)	
Charlson comorbidity index	0	2956	554 (18.7)	0.080
	1	1018	202 (19.8)	
	≥2	273	66 (24.2)	
Race	White	3366	661 (19.6)	0.932
	Black	307	57 (18.6)	
	Hispanic	356	64 (18.0)	
	Asian	186	34 (18.3)	
	Other	32	6 (18.8)	
Marital status	Unmarried	605	102 (16.9)	0.031
	Married	3469	694 (20.0)	
	Unknown	173	26 (15.0)	
Education: % of census tract with at least a high school degree	<75	785	142 (18.1)	0.108
	75–84.99	785	131 (16.7)	
	85–89.99	791	159 (20.1)	
	≥90	1885	389 (20.6)	
Median income in census tract of residence	<$35 000	1106	203 (18.35)	0.321
	$35 000–44 000	975	188 (19.28)	
	$45 000–59 000	1072	227 (21.18)	
	≥$60 000	1093	203 (18.57)	
SEER region	San Francisco	171	31 (18.13)	<0.001
	Detroit	303	59 (19.47)	
	Iowa	195	46 (23.6)	
	Seattle	352	85 (24.15)	
	Utah	284	78 (27.5)	
	Connecticut	127	27 (21.26)	
	San Jose	103	21 (20.39)	
	Los Angele	569	137 (24.08)	
	Greater Ca	1171	232 (19.81)	
	Kentucky	215	31 (14.42)	
	Louisiana	316	43 (13.61)	
	New Jersey	265	13 (4.9)	
	New Mexico/Georgia/Hawaii	176	19 (10.80)	
Population density	Metropolitan	3989	773 (19.38)	0.891
	Rural	258	49 (18.99)	
Clinical stage	T1c	2218	408 (18.39)	0.452
	T2	737	148 (20.08)	
	T3	39	9 (23.08)	
	Unknown	1253	257 (20.51)	
Gleason grade	≤ 6	1687	190 (11.26)	<0.001
	7	2073	487 (23.49)	
	≥8	469	144 (30.70)	
	Unknown	18	1 (5.56)	
PSA	<10	3141	568 (18.08)	0.0001
	10–20	495	123 (24.85)	
	>20	170	47 (27.65)	
	Unknown	441	84 (19.05)	
D'Amico risk	Low	1242	130 (10.47)	<0.001
	Intermediate	2265	502 (22.16)	
	High	637	177 (27.79)	
	Unknown	103	13 (12.62)	

PSA, prostate-specific antigen; SEER, surveillance, epidemiology, and end results.

TABLE 2 Surgical margin status by surgeon volume, surgical approach and pathological stage

Independent variable	Category	Total	Positive margin *n* (%)	*P*-value
Surgical approach	MIRP	1121	195 (17.4)	0.086
	RRP	3119	627 (20.1)	
Surgeon volume in quartiles (no. of surgeons by approach)	Low (MIRP 85; RRP 396)	1027	179 (17.43)	0.329
	Intermediate (MIRP 21; RRP 169)	1130	217 (19.20)	
	High (MIRP 12; RRP 91)	1159	228 (19.67)	
	Very high (MIRP < 11*; RRP 37)	931	198 (21.27)	
Pathological stage	T2	3544	528 (14.9)	<0.001
	T3a	700	294 (42.0)	

MIRP, minimally invasive radical prostatectomy; RRP, radical retropubic prostatectomy.
**Actual number of MIRP surgeons not presented because the National Cancer Institute precludes the reporting of table cells of n < 11.*

Categorically, surgeon volume for the study period was divided into quartiles, consistent with a previous study [12], corresponding to 1–7 radical prostatectomies for low, 8–15 for intermediate, 16–29 for high, and 30–91 for very high for open radical prostatectomy surgeons. On the other hand, the minimally invasive radical prostatectomy surgeon volume quartile distribution over the study period was 1–14 radical prostatectomies for low, 15–36 for intermediate, 37–89 for high, and 90–218 for very high volume surgeons.

In sub-analyses, we analysed the effect of surgeon volume on minimally invasive and open radical prostatectomy surgical margin positivity, respectively, and did not find a significant relationship. Finally, we stratified surgical approach into minimally invasive vs open radical prostatectomy.

Bivariate analyses were performed to compare patient characteristics and positive surgical margin status by surgeon volume using the Rao-Scott–Pearson chi-squared statistic, which accounts for clustering by surgeon [13]. A Rao-Scott–Pearson chi-squared test was also used to compare the overall positive margin by surgical approach. Logistic regression was performed to determine the effect of surgeon volume as a continuous and categorical variable; logistic regression was also used to assess the effect of age, race, SEER region, surgical approach, D'Amico risk stratification, and year of surgery on positive surgical margins. For the logistic regressions, generalized estimating equations were used to account for clustering of patients by surgeon [14]. All tests were considered statistically significant at $\alpha = 0.05$.

All analyses were performed with SAS version 9.1.3 (SAS Institute, Cary, NC, USA).

To derive the 25th and 10th percentile positive surgical margin thresholds for a given urologist, using results from generalized linear mixed models (given a random urologist effect) [15], the number of operations with positive margins out of the N operations performed by a surgeon follows a binomial distribution. Because most practicing urologists perform fewer than 12 major operations a year including radical prostatectomy [16], we present postivie surgical margin performance thresholds for surgeon volumes of 5 to 12 radical prostatectomies. Moreover, given that 42% [17] of US radical prostatectomies are performed in men aged 65 years and older, we determined that 57.6% and 67.7% of minimally invasive radical prostatectomy surgeons performed fewer than 12 radical prostatectomies in 2004 and 2005 whereas 67.6% and 70.5% of open radical prostatectomy surgeons performed fewer than 12 radical prostatectomies in 2004 and 2005, respectively. Assuming that the probability of a positive margin equals the mean positive margin rate from our study population, the 25th and 10th percentiles for surgeon-specific positive margin rates out of N operations performed can be derived using the binomial distribution formula [18], with π as the mean population-based positive margin rate, and N as the number of operations performed. The exact percentiles can be obtained from the SAS 'quantile' function. A normal-based approximation to the percentiles can be obtained with the formulae [19]:

$$25\text{th percentile} = \pi + 1.5/N + 0.675\sqrt{\pi(1-\pi)/N}$$

$$10\text{th percentile} = \pi + 1.5/N + 1.28\sqrt{\pi(1-\pi)/N}$$

RESULTS

The demographics of our study population are presented in Table 1. The positive surgical margin rate decreased during the 3-year study period from 21.3% to 16.6% from 2004 to 2006. Although there were no significant associations between age, comorbidity and race and positive surgical margins, married men were more likely than unmarried men to experience positive surgical margins (20.0% vs 16.9%, $P = 0.031$). Moreover, there was significant geographic variation in positive surgical margin rates, ranging from 4.9% to 27.5% ($P < 0.001$). Finally, higher PSA level ($P < 0.001$) and Gleason grade ($P < 0.001$), and consequently higher risk disease ($P < 0.001$), were associated with higher positive surgical margin rates.

The relationships between surgical approach, surgeon volume and pathological stage with positive surgical margins are presented in Table 2. There was a trend for fewer positive surgical margins with minimally invasive vs retropubic radical prostatectomy (20.1% vs 17.4%, $P = 0.086$) but there was no association between overall surgeon volume with positive surgical margins. In addition, sub-analyses of minimally invasive and retropubic radical prostatectomy surgeon volume, respectively, did not reveal an association with positive surgical margins.

However, the positive surgical margin rate was higher for pT3a vs pT2 disease (42.0% vs 14.9%, $P < 0.001$).

The adjusted analyses are presented in Table 3. Men undergoing radical prostatectomy in 2005 vs 2004 experienced lower odds for positive surgical margins (odds ratio 0.83, 95% CI 0.7–0.98), and there was a trend for lower odds of positive surgical margins in 2006 vs 2004 (OR 0.75, 95% CI 0.55–1.01). Significant geographic variation in positive surgical margin rates persisted in adjusted analysis. Whereas men undergoing radical prostatectomy in New Jersey experienced lower odds of positive surgical margins (OR 0.23, 95% CI 0.12–0.43), those in Utah (OR 1.94, 95% CI 1.17–3.22) and Los Angeles (OR 1.56, 95% CI 1.01–2.42) experienced greater odds of positive surgical margins vs San Francisco (referent). Moreover, men with high-risk (OR 3.68 95% CI 2.82–4.81) and intermediate-risk (OR 2.52, 95% CI 2.03–3.13) vs low-risk features experienced greater odds of positive surgical margins. Notably, there was no association between surgeon volume stratified in quartiles and assessed as a continuous variable (Appendix) and likelihood of positive surgical margins.

Table 4 displays the 25th and 10th percentile positive margin rate thresholds for organ-confined disease based on the population-based pT2 positive margin rate of 14.9%. This is derived from the exact binomial for $\pi = 0.149$ and varying surgeon volumes (N). For example, a surgeon experiencing positive margins in 3 of 10 men with organ-confined disease would perform at the 25th percentile.

TABLE 3 Adjusted model for predictors of surgical margin positivity

Covariate (referent)	Categories	OR (95% CI)	*P*-value
Age (≥75 years)	65–69	1.01 (0.69–1.46)	0.978
	70–74	1.03 (0.71–1.48)	0.877
Race (White)	Black	1.19 (0.84–1.69)	0.333
	Hispanic	0.91 (0.68–1.23)	0.547
	Asian	0.88 (0.58–1.34)	0.556
D'Amico risk (Low)	Intermediate	2.52 (2.03–3.13)	<0.001
	High	3.68 (2.82–4.81)	<0.001
Surgical approach (RRP)	MIRP	0.93 (0.77–1.13)	0.464
Surgeon volume (Low)	Intermediate	1.0 (0.77–1.3)	0.989
	High	0.94 (0.74–1.18)	0.583
	Very high	1.02 (0.8–1.31)	0.845
SEER Region (San Francisco)	Detroit	1.16 (0.72–1.86)	0.534
	Iowa	1.41 (0.82–2.4)	0.213
	Seattle	1.43 (0.9–2.28)	0.125
	Utah	1.94 (1.17–3.22)	0.011
	Connecticut	1.23 (0.72–2.11)	0.451
	San Jose	1.24 (0.7–2.19)	0.460
	Los Angeles	1.56 (1.01–2.42)	0.047
	Greater California	1.17 (0.78–1.77)	0.440
	Kentucky	0.73 (0.42–1.26)	0.254
	Louisiana	0.68 (0.39–1.17)	0.160
	New Jersey	0.23 (0.12–0.43)	<0.001
	New Mexico/Georgia/Hawaii	0.54 (0.28–1.05)	0.071
Year (2004)	2005	0.83 (0.7–0.98)	0.033
	2006	0.75 (0.55–1.01)	0.057

95% CI, 95% confidence interval; MIRP, minimally invasive radical prostatectomy; OR, odds ratio; RRP, radical retropubic prostatectomy.

TABLE 4 Positive surgical margin percentile thresholds for surgeon volume of 5 to 12 radical prostatectomies based on binomial distribution and population means for pT2 and pT3a disease

Surgeon volume	Organ-confined disease, $\pi = 0.0149$ *n* cases with positive margins (%)		Extracapsular extension, $\pi = 0.420$ *n* cases with positive margins (%)	
N	25th percentile	10th percentile	25th percentile	10th percentile
5	2 (40)	3 (60)	4 (80)	5 (100)
6	2 (33)	3 (50)	4 (67)	5 (83)
7	3 (43)	3 (43)	5 (71)	6 (86)
8	3 (38)	4 (50)	5 (63)	6 (75)
9	3 (33)	4 (44)	6 (67)	7 (78)
10	3 (30)	4 (40)	6 (60)	7 (70)
11	3 (27)	4 (36)	7 (64)	8 (73)
12	4 (33)	5 (41)	7 (58)	8 (67)

Because of the discreteness of the binomial distribution, the cutoff rates are not identical for different surgeon volumes. Using the n values in this table, the 25th and 10th percentiles are actually (n – 1)/N, but to reduce confusion, because correction action may be undertaken if surgeon-specific positive margin rates exceed the 25th percentiles, this table includes the minimum thresholds for the above percentiles.

DISCUSSION

Population-based studies have shown that higher radical prostatectomy surgeon volume is associated with fewer in-hospital and late urinary complications, shorter lengths of stay, and less use of additional cancer therapy [4,11,12]. In addition, multicentre studies have characterized a learning curve for cancer control, as greater surgeon experience in open and minimally invasive radical prostatectomies portends fewer biochemical recurrences [20,21]. A recent population-based study showed significantly greater use of additional cancer treatments, i.e. radiation and/or hormonal therapy, within 6 months of minimally invasive vs open radical prostatectomy but potential confounders

such as surgical margin status and pathological stage and grade were unavailable [4]. Additionally, there is an absence of population-based studies that explore the potential influence of surgical approach and surgeon volume on positive margin status. Positive surgical margins increase patient distress and fear of cancer recurrence [22], and add to healthcare costs when adjuvant radiotherapy is added to improve cancer control [2,3].

Our paper has several important findings. First, we present population-based radical prostatectomy positive surgical margin rates of 14.9% for organ-confined disease and 42% for extracapsular extension. In addition, we derived positive surgical margin performance thresholds that may serve as benchmarks for surgeon self-assessment, rather than comparison with published positive margin rates from high-volume single surgeon series. Surgeons experiencing positive margin rates in excess of population-based benchmarks might review intraoperative video of themselves [23] or others and seek courses to improve their surgical technique and lower their positive margin rates. Although we present 25th and 10th percentile population-based positive margin thresholds, others may use the binomial distribution to individualize 'acceptable' performance levels.

Second, we observed lower positive surgical margin rates when comparing radical prostatectomies performed in 2005 vs 2004. There was a trend for lower positive surgical margin rates for 2006 than 2004 but the study might have been underpowered to detect significance because our study cohort comprised men diagnosed with prostate cancer through 2005 who had surgery in 2006, rather than including all men undergoing radical prostatectomy in 2006. Although a temporal trend for fewer positive surgical margins is consistent with the gradual diffusion of surgical technique and improved outcomes that follow [24,25], subsequent years of data, when available, must be analysed to determine if margin rates continue to decrease.

Third, we observed significant geographic variation in positive surgical margin rates. This parallels variations in positive surgical margin rates from single centre reports. Moreover, our regional differences in positive surgical margins parallel other population-based studies showing geographic variation in radical prostatectomy outcomes [11,24,26]. These findings underscore the heterogeneity in radical prostatectomy technique and outcomes. Moreover, we observed that married vs unmarried men experienced high surgical margin positivity; however, the inability to determine use of nerve-sparing technique from SEER-Medicare data prevents us from exploring this further.

Fourth, while there are purported advantages of tumour palpation and intraoperative decision-making on improved cancer control during open compared with minimally invasive radical prostatectomy [6], most US men with prostate cancer increasingly present with raised PSA levels and low-volume disease rather than with disease that is palpable on digital rectal examinations [10,27], and our population-based analyses show similar positive surgical margin rates between minimally invasive and open radical prostatectomy. Moreover, early cancer control was also similar for minimally invasive and open radical prostatectomy from a study of SEER-Medicare linked data [7]. Our findings contrast with those contending that men undergoing minimally invasive vs open radical prostatectomy experience inferior cancer control [4,28].

Finally, we did not observe a relationship between surgeon volume and positive surgical margin status. This contrasts two multicentre studies showing that higher surgeon volume was associated with lower positive margin rates [29,30]. However, individual surgeon characteristics and heterogeneity also affect surgical margin status; surgeon volume was no longer a predictor of surgical margin status after excluding the highest volume surgeon from one study [30] but positive margin rates for open radical prostatectomy surgeons at high volume, academic referral centres varied widely from 11% to 48% in the other study [29]. In addition, a recent multicentre study showed significant heterogeneity in cancer recurrence after adjusting for surgeon experience and tumour characteristics [31].

Our findings must be interpreted in the context of the study design. First, SEER-Medicare does not contain detailed clinical information regarding whether nerve-sparing technique was used, which increases the likelihood of positive surgical margins [32]. Second, Medicare is limited to men aged 65 years and older, and nerve-sparing may be performed more frequently in younger, potent men [32]. This, along with the absence of margin status for pathological T3b and T4 disease, may lead to underestimation of the overall prevalence of positive margins in all men undergoing radical prostatectomy, regardless of age. However, the number of men omitted with pathological T3b and T4 disease was relatively small, and positive margins in organ-confined vs extraprostatic disease may serve as a better litmus test for the quality of surgical technique. Third, heterogeneous pathological processing and interpretation may lead to variation in positive surgical margin status [2,3]. Fourth, we were unable to differentiate between minimally invasive radical prostatectomy performed with and without robotic assistance because both share a common CPT code; however, a recent survey showed a 75% reduction in volume among surgeons performing minimally invasive radical prostatectomy without robotic assistance [33], and the robot-assisted approach likely accounted for most of the minimally invasive radical prostatectomies. Finally, many cases and several years may transpire before low-volume surgeons can accurately characterize their positive margin rates stratified by tumour characteristics, and this may be a potential limitation of our margin positivity thresholds for surgical margin positivity because real-time feedback is unavailable.

Our population-based, organ confined (pT2) positive surgical margin rate of 14.9% and 25th and 10th percentile cutoffs may serve as a benchmark for radical prostatectomy surgeon self-assessment. Although we observed temporal improvement and significant geographic variation in positive surgical margin rates, we did not find a surgeon volume–outcomes effect with positive surgical margins, probably because of heterogeneity in the surgical technique. Finally, positive surgical margin rates were similar for minimally invasive and open radical prostatectomy.

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CONFLICT OF INTEREST

None declared.

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Abbreviations: **OR**, odds ratio; **SEER**, surveillance, epidemiology, and end results.

APPENDIX ADJUSTED MODEL OF PREDICTORS OF SURGICAL MARGIN POSITIVITY WITH SURGEON VOLUME AS A CONTINUOUS VARIABLE

Covariate (referent)	Categories	OR (95% CI)	*P*-value
Age (≥75 years)	65–69	1.01 (0.69–1.47)	0.975
	70–74	1.03 (0.71–1.49)	0.874
Race (White)	Black	1.19 (0.84–1.69)	0.335
	Hispanic	0.92 (0.68–1.24)	0.569
	Asian	0.89 (0.59–1.34)	0.567
D'Amico risk (Low)	Intermediate	2.5 (2.03–3.13)	<0.001
	High	3.7 (2.81–4.80)	<0.001
Surgical approach (RRP)	MIRP	0.91 (0.72–1.14)	0.404
Surgeon volume (continuous)	Per 10 surgeries	1.01 (0.99–1.02)	0.512
SEER region	Detroit	1.14 (0.72–1.82)	0.570
	Iowa	1.4 (0.82–2.38)	0.217
	Seattle	1.43 (0.91–2.25)	0.119
	Utah	1.91 (1.15–3.17)	0.012
	Connecticut	1.24 (0.73–2.12)	0.421
	San Jose	1.23 (0.7–2.19)	0.469
	Los Angeles	1.55 (1–2.4)	0.051
	Greater California	1.17 (0.78–1.75)	0.445
	Kentucky	0.73 (0.42–1.25)	0.251
	Louisiana	0.68 (0.4–1.15)	0.152
	New Jersey	0.23 (0.12–0.43)	<0.001
	New Mexico/Georgia/Hawaii	0.55 (0.28–1.06)	0.074
Year (2004)	2005	0.83 (0.7–0.98)	0.033
	2006	0.75 (0.56–1.01)	0.059

95% CI, 95% confidence interval; MIRP, minimally invasive radical prostatectomy; OR, odds ratio; RRP, radical retropubic prostatectomy.

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Original article

The effect of minimally invasive and open radical prostatectomy surgeon volume

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Abstract

Objective: To determine the effect of minimally invasive radical prostatectomy (MIRP) surgeon volume on outcomes, and correlate with those of open radical prostatectomy retropubic (ORP).

Methods and materials: Observational population-based study of 8,831 men undergoing MIRP and ORP by 1,457 low, medium, and high volume surgeons from SEER-Medicare linked data from 2003 to 2007. After stratifying by surgeon ORP and MIRP volume, the following outcomes were studied: length of stay, transfusions, post-operative 30-day and anastomotic stricture complications, and use of additional cancer therapies.

Results: Men undergoing MIRP with high and medium vs. low volume surgeons were less likely to require additional cancer therapies (4.5% and 4.7% vs. 7%, $P = 0.020$). Similarly, men undergoing ORP with high vs. medium and low volume surgeons were less likely to require additional cancer therapies (5.7% vs. 6.8% and 7.1%, $P = 0.044$). Men undergoing ORP with high vs. medium and low volume surgeons experienced shorter lengths of stay (2.9 vs. 3.3 and 3.6 days, $P < 0.001$), and fewer transfusions (15.4% vs. 21.3% and 22.7%, $P = 0.017$), 30-day complications (18.4% vs. 25.6% and 25.7%, $P < 0.001$), and anastomotic strictures (10.1% vs. 15.6% and 16.3%, $P = 0.003$). However, MIRP surgeon volume did not affect these outcomes.

Conclusions: Men undergoing MIRP or ORP with high volume surgeons were less likely to require additional cancer therapies. Additionally, patients of high volume ORP surgeons were more likely to experience shorter hospital stays, fewer transfusions, 30-day complications, and anastomotic strictures, while MIRP surgeon volume did not affect these peri-operative outcomes.

Keywords: Surgeon volume; Surgical outcomes; Radical prostatectomy; Robotic surgery

1. Introduction

Volume-outcome effects, the association between higher volume and better outcomes, have been established for many surgical procedures [1], providing the rationale for using volume as a proxy for quality. Defining quality indicators is a prerequisite for the implementation of pay-for-performance programs, an essential pillar of current U.S. healthcare reform initiatives. Radical prostatectomy is the most common oncologic operation performed by urologists with more than 60,000 procedures performed annually in the U.S. [2]. Several studies have demonstrated an association between higher open radical retropubic prostatectomy (ORP) surgeon volume and better outcomes [3,4], and surgeon volume is a prostate cancer quality indicator [5]. Further, to increase transparency and improve quality-of-care,

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Table 1
Demographic and tumor characteristics by MIRP and ORP surgeon volume

Variable	Categories	Before propensity weighting				After propensity weighting			
		MIRP surgeon volume				MIRP surgeon volume			
		Low $n = 211$	Medium $n = 34$	High $n = 11$	P value	Low $n = 211$	Medium $n = 34$	High $n = 11$	P value
Age (years)	65–69	374 (61.0%)	394 (64.1%)	386 (56.2%)	<0.001	373 (61.5%)	370 (60.3%)	439 (63.2%)	0.940
	70–74	201 (32.8%)	188 (30.6%)	229 (33.3%)		192 (31.7%)	197 (32.2%)	208 (29.9%)	
	75+	38 (6.2%)	33 (5.4%)	72 (10.5%)		41 (6.8%)	46 (7.5%)	48 (6.8%)	
Charlson score	0	427 (69.7%)	442 (71.9%)	497 (72.3%)	0.676	429 (70.7%)	437 (71.3%)	510 (73.5%)	0.842
	1	142 (23.2%)	141 (22.9%)	145 (21.1%)		140 (23.1%)	134 (21.8%)	144 (20.7%)	
	2+	44 (7.2%)	32 (5.2%)	45 (6.6%)		37 (6.1%)	42 (6.9%)	40 (5.8%)	
Race	White	492 (80.3%)	508 (82.6%)	551 (80.2%)	0.852	493 (81.4%)	491 (80.1%)	553 (79.6%)	0.999
	Black	38 (6.2%)	35 (5.7%)	42 (6.1%)		38 (6.3%)	37 (6.1%)	41 (5.9%)	
	Hispanic	43 (7.0%)	26 (4.2%)	37 (5.4%)		31 (5.1%)	36 (5.9%)	39 (5.6%)	
	Asian	29 (4.7%)	36 (5.9%)	52 (7.6%)		35 (5.7%)	39 (6.4%)	52 (7.5%)	
Marital status	Not married	91 (14.9%)	70 (11.4%)	96 (14.0%)	0.170	82 (13.5%)	83 (13.5%)	87 (12.5%)	0.738
	Married	467 (76.2%)	466 (75.8%)	551 (80.2%)		471 (77.6%)	474 (77.3%)	516 (74.3%)	
	Unknown	55 (9.0%)	79 (12.9%)	40 (5.8%)		53 (8.8%)	56 (9.1%)	92 (13.2%)	
% with at least a high school education in census tract of residence	<75	124 (20.3%)	76 (12.4%)	77 (11.2%)	<0.001	91 (15.1%)	93 (15.1%)	109 (15.8%)	0.999
	75–84.9	120 (19.6%)	119 (19.4%)	111 (16.2%)		109 (18%)	112 (18.2%)	120 (17.3%)	
	85–89.9	127 (20.8%)	103 (16.8%)	93 (13.5%)		100 (16.5%)	103 (16.7%)	110 (15.9%)	
	90+	241 (39.4%)	317 (51.5%)	406 (59.1%)		306 (50.5%)	306 (49.9%)	354 (51.1%)	
Median household income ($) in census tract of residence	<35,000	163 (26.6%)	107 (17.4%)	84 (12.2%)	<0.001	112 (18.5%)	117 (19.1%)	138 (19.9%)	0.999
	35–44,999	146 (23.9%)	141 (22.9%)	111 (16.2%)		128 (21.1%)	124 (20.2%)	139 (20%)	
	45–59,999	137 (22.4%)	152 (24.7%)	183 (26.6%)		144 (23.8%)	155 (25.3%)	167 (24%)	
	≥60,000	166 (27.1%)	215 (35.0%)	309 (45.0%)		222 (36.6%)	217 (35.4%)	251 (36.1%)	
Population density	Metropolitan	559 (91.2%)	580 (94.3%)	684 (99.6%)	<0.001	577 (95.2%)	582 (94.9%)	653 (94%)	0.919
AJCC pathologic stage	T2	409 (66.7%)	420 (68.3%)	479 (69.7%)	0.396	420 (69.3%)	416 (67.8%)	462 (66.5%)	0.975
	≥T3	111 (18.1%)	120 (19.5%)	128 (18.6%)		108 (17.8%)	113 (18.4%)	124 (17.7%)	
	Other	93 (15.2%)	75 (12.2%)	80 (11.6%)		78 (12.9%)	84 (13.7%)	109 (15.7%)	
Tumor grade	Well/moderately differentiated	283 (46.2%)	300 (48.8%)	355 (51.7%)	0.425	302 (49.8%)	302 (49.3%)	355 (51.2%)	0.989
	Poorly/undifferentiated	323 (52.7%)	309 (50.2%)	330 (48.0%)		300 (49.5%)	306 (49.9%)	335 (48.2%)	

Table 1
Continued

Variable	Categories	Before propensity weighting				After propensity weighting			
		ORP surgeon volume				ORP surgeon volume			
		Low $n = 879$	Medium $n = 236$	High $n = 86$	*P* value	Low $n = 879$	Medium $n = 236$	High $n = 86$	*P* value
Age (years)	65–69	1604 (67.4%)	1453 (61.6%)	1293 (59.4%)	<0.001	1497 (63%)	1481 (62.8%)	1374 (63.1%)	0.999
	70–74	671 (28.2%)	749 (31.8%)	680 (31.2%)		724 (30.5%)	717 (30.4%)	656 (30.1%)	
	75+	105 (4.4%)	156 (6.6%)	204 (9.4%)		156 (6.6%)	160 (6.8%)	147 (6.8%)	
Charlson score	0	1598 (67.1%)	1628 (69.0%)	1527 (70.1%)	0.317	1626 (68.4%)	1617 (68.6%)	1493 (68.5%)	0.999
	1	622 (26.1%)	567 (24.1%)	522 (24.0%)		594 (25%)	586 (24.9%)	544 (25%)	
	2+	160 (6.7%)	163 (6.9%)	128 (5.9%)		157 (6.6%)	155 (6.6%)	141 (6.5%)	
Race	White	1861 (78.2%)	1867 (79.2%)	1810 (83.1%)	0.482	1893 (79.6%)	1886 (80%)	1730 (79.5%)	0.999
	Black	194 (8.2%)	197 (8.4%)	138 (6.3%)		190 (8%)	180 (7.6%)	178 (8.2%)	
	Hispanic	202 (8.5%)	195 (8.3%)	150 (6.9%)		191 (8%)	189 (8%)	175 (8.1%)	
	Asian	85 (3.6%)	75 (3.2%)	59 (2.7%)		76 (3.2%)	75 (3.2%)	69 (3.2%)	
Marital status	Not married	384 (16.1%)	352 (14.9%)	321 (14.8%)	0.005	369 (15.5%)	362 (15.3%)	342 (15.7%)	0.999
	Married	1840 (77.3%)	1915 (81.2%)	1778 (81.7%)		1898 (79.8%)	1885 (79.9%)	1736 (79.7%)	
	Unknown	156 (6.6%)	91 (3.9%)	78 (3.6%)		110 (4.6%)	111 (4.7%)	100 (4.6%)	
% with at least a high school education in census tract of residence	<75	548 (23.1%)	472 (20.0%)	348 (16.0%)	<0.001	479 (20.2%)	467 (19.8%)	443 (20.4%)	0.999
	75–84.9	516 (21.7%)	498 (21.1%)	365 (16.8%)		472 (19.9%)	469 (19.9%)	426 (19.6%)	
	85–90	444 (18.7%)	467 (19.8%)	405 (18.6%)		444 (18.7%)	448 (19%)	409 (18.8%)	
	>90	867 (36.5%)	920 (39.0%)	1057 (48.6%)		981 (41.3%)	972 (41.2%)	897 (41.2%)	
Median household income ($) in census tract of residence	<35,000	762 (32.1%)	776 (32.9%)	580 (26.7%)	0.151	740 (31.1%)	725 (30.8%)	670 (30.8%)	0.999
	35–44,999	546 (23.0%)	557 (23.6%)	556 (25.6%)		559 (23.5%)	563 (23.9%)	525 (24.1%)	
	45–59,000	586 (24.75)	532 (22.6%)	508 (23.4%)		564 (23.7%)	556 (23.6%)	511 (23.5%)	
	≥60,000	481 (20.3%)	492 (20.9%)	531 (24.4%)		513 (21.6%)	513 (21.8%)	470 (21.6%)	
Population density	Metropolitan	2138 (89.8%)	2134 (90.5%)	2041 (93.8%)	0.087	2171 (91.3%)	2153 (91.3%)	1987 (91.2%)	0.999
AJCC pathologic stage	T2	1414 (59.4%)	1426 (60.5%)	1322 (60.7%)	<0.001	1430 (60.2%)	1420 (60.2%)	1305 (59.9%)	0.999
	≥T3	576 (24.2%)	632 (26.1%)	610 (28.0%)		625 (26.3%)	620 (26.3%)	579 (26.5%)	
	Other	390 (16.4%)	300 (12.7%)	245 (11.3%)		322 (13.5%)	318 (13.5%)	294 (13.5%)	
Tumor grade	Well/moderately differentiated	1226 (51.5%)	1170 (49.6%)	1115 (51.2%)	0.147	1213 (51%)	1194 (50.6%)	1112 (51.1%)	0.997
	Poorly/undifferentiated	1132 (47.6%)	1177 (49.9%)	1055 (48.5%)		1151 (48.4%)	1152 (48.8%)	1052 (48.3%)	

state governments have publicized radical prostatectomy surgeon volumes [6]. However, in 2005, 80% of U.S. urologists performed fewer than 10 radical prostatectomies per year, and 25% performed just 1 [7].

Minimally invasive radical prostatectomy (MIRP)—that is, laparoscopic radical prostatectomy with or without robotic assistance—has experienced rapid and widespread diffusion [8,9]. To perform robotic-assisted MIRP, there are few barriers to entry: urologists must attend a 2-day course before scheduling cases supervised by proctors who have performed at least 20 robotic-assisted MIRP. Requirements may be less rigorous for attaining hospital privileges for MIRP without robotic assistance. For these reasons, concern has been raised that outcomes may be sacrificed during the initiation of a MIRP program [10]. While previous studies directly compared MIRP vs. ORP outcomes [11], not much is known about how MIRP volume affects outcomes, and if this differs from the way ORP volume affects outcomes. The purpose of our population-based study is 2-fold: (1) to delineate surgeon volume-outcome effects for MIRP and ORP, and (2) to compare the volume-outcome effects for MIRP vs. ORP.

2. Materials and methods

Our study was approved by the Brigham and Women's Institutional Review Board. Patient data were de-identified and the requirement for consent was waived. We used Surveillance, Epidemiology, and End Results (SEER)-Medicare linked data for analyses. Medicare provides benefits to 97% of Americans aged ≥65 years, and SEER provides cancer-specific registry data to 93% of Medicare beneficiaries. Together, SEER-Medicare comprises approximately 26% of the U.S. population [12].

We identified men aged ≥65 years with complete Medicare coverage who were diagnosed with nonmetastatic prostate cancer from 2002 to 2005 as their only cancer. Men who underwent ORP and MIRP from 2003 to 2006 (n = 8,831) were identified based on the presence of Current Procedural Terminology 4th Edition (CPT-4) codes 55840, 55842, 55845 for ORP, and 55866 for MIRP. Demographic and tumor characteristics were obtained from SEER registry data, while patient age was obtained from the Medicare file. Comorbidity was assessed using the Klabunde modification of the Charlson index based on claims submitted during the year prior to surgery [13].

We examined mortality/morbidity, length of stay, use of cystography, anastomotic strictures, and use of additional cancer therapy (Appendix A), [3,4,8,9]. Postoperative mortality, complications, heterologous transfusions, and use of cystography were captured up to 30 days after surgery. Complication categories included cardiac, respiratory, genitourinary, vascular, wound, and miscellaneous medical and surgical. Anastomotic strictures were assessed from 31 to 365 days after surgery [4]. Long term incontinence [4] and erectile dysfunction [14] were captured on the basis of symptoms leading to a diagnosis or procedures to treat these conditions more than 18 months after surgery, the interim required for recovery of postoperative urinary and sexual function to plateau [15]. We identified men undergoing additional post-prostatectomy cancer therapy (radiation, hormonal therapy) [8], a measure of cancer control.

Because surgeon rather than hospital volume mediates ORP outcomes [3], we determined surgeon volume for each type of procedure by aggregating the number of prostatectomies performed from 2003 to 2006. While we originally stratified surgeon volume into quartiles [4], this resulted in potential confidentiality issues, and we consequently stratified surgeon volume into tertiles (low, medium, high). For men with more than 1 surgeon listed, we selected the surgeon who performed the larger volume of radical prostatectomies for analysis [4].

Unadjusted univariate analysis was performed to compare patient characteristics by surgical approach using the Pearson χ^2 statistic. For dichotomous outcomes such as complications, we compared unadjusted proportions of interest among men undergoing MIRP and ORP, using the Pearson χ^2 statistic. For dichotomous outcome variables in which patients had varying length of follow-up, we compared rates (number of events per 100 person-years follow-up). Generalized estimating equations (GEE) [16] were used to account for surgeon clustering in unadjusted and adjusted analyses. To compare unadjusted proportions and rates, we fit GEE logistic regressions and GEE log-linear Poisson regression, respectively, with surgeon volume as the only covariate.

In adjusted analyses, we used weighted propensity score methods to adjust for possible confounders when examining the effect of surgeon volume on outcomes [17]. Propensity score methods permit control for all observed confounding factors that might influence group assignment and outcome using a single composite measure. In addition, it attempts to balance patient characteristics between groups, as would occur in a randomized experiment. Covariate balance was checked after adjustment (Table 1, weighted values). All tests were considered statistically significant at $\alpha = 0.05$. Analyses were performed with SAS ver. 9.1.3 (SAS Institute, Cary, NC).

3. Results

The demographics of our study population are shown in Table 1. A total of 6,915 men underwent ORP by 1,201 surgeons, and 1,915 men underwent MIRP by 256 surgeons. The MIRP volume tertiles correspond to 1–17 (low), 18–52 (medium), 53–424 (high), patients per surgeon, while the ORP volume categories correspond to 1–11 (low), 12–25 (medium), 26–94 (high) patients per surgeon during the study period. Assuming that 42% of patients undergoing prostatectomy are aged ≥65 years [18], we project that these ranges correspond to total annual volumes of 1–10,

Table 2
Unadjusted association of MIRP and RRP surgeon volume and outcomes

Variable	MIRP surgeon volume tertile				ORP surgeon volume tertile			
	Low $n = 211$	Medium $n = 34$	High $n = 11$	P value	Low $n = 879$	Medium $n = 236$	High $n = 86$	P value
Transfusion	3.3%	2.0%	1.6%	0.274	22.7%	21.3%	15.6%	0.014
Overall complication	21.7%	21.1%	22.4%	0.921	25.5%	25.8%	18.7%	<0.001
Cardiac	2.3%	2.3%	1.9%	0.835	3.5%	2.9%	3.2%	0.554
Respiratory	5.4%	3.7%	3.6%	0.252	8.4%	6.8%	4.9%	<0.001
Genitourinary	2.6%	1.5%	3.1%	0.157	1.6%	1.2%	1.1%	0.274
Wound	<1.9%*	<1.9%*	2.2%	0.021	1.9%	2.1%	1.0%	0.014
Vascular	2.3%	4.1%	2.0%	0.060	4.4%	3.9%	3.4%	0.223
Miscellaneous medical	9.8%	10.1%	7.4%	0.319	9.7%	9.3%	6.9%	0.012
Miscellaneous surgical	4.7%	4.9%	4.5%	0.961	5.8%	6.8%	3.7%	<0.001
Length of stay†	2.3	1.9	1.8	0.016	3.6	3.3	2.8	<0.001
Stricture	6.4%	4.6%	5.4%	0.523	16.4%	15.7%	9.7%	<0.001
Additional cancer therapy‡	7.2	4.6	4.8	0.012	7	7	5.8	0.067
Cystography	25.6%	22.1%	44.8%	0.019	9.4%	7.1%	13.8%	0.065

* The exact percentage is not reported due to potential confidentiality issues.
† Mean ratios.
‡ Rate per 100 person years, follow-up until 12/31/2006.

11–31, and 32–252 procedures per surgeon for MIRP, and 1–6, 7–15, and 16–56 for ORP.

High volume MIRP surgeons were more likely to operate on older men ($P < 0.001$) in metropolitan ($P < 0.001$) census tracts with higher education ($P < 0.001$) and income ($P < 0.001$). Similarly, high volume ORP surgeons were more likely to operate on older men ($P < 0.001$), married men ($P = 0.005$), and those of higher education ($P < 0.001$). High volume ORP surgeons were more likely to operate on men with at least pathologic T3 disease ($P < 0.001$).

The unadjusted comparison of outcomes by surgeon volume and surgical approach is shown in Table 2. There were only 13 peri-operative deaths (0.15%), too few to stratify by surgeon volume. In unadjusted analyses, patients of high volume MIRP surgeons were more likely to undergo cystograms ($P = 0.019$), experience shorter lengths of stay ($P = 0.016$), have fewer wound complications ($P = 0.021$), and are less likely to receive additional cancer therapy ($P = 0.012$). In adjusted analyses (Table 3), men of high volume MIRP surgeons were less likely to require additional cancer therapy only ($P = 0.020$).

In contrast to MIRP, unadjusted analyses revealed that overall 30-day, respiratory, wound, miscellaneous medical and surgical, transfusion, and anastomotic stricture complications were lowest for high volume ORP surgeons ($P < 0.05$, respectively). In addition, patients of high volume ORP surgeons experienced shorter lengths of stay ($P < 0.001$). In adjusted analyses of ORP surgeon volume-outcome effects, all of the associations above remained signif-

Table 3
Adjusted association of MIRP and RRP surgeon volume and outcomes

Variable	MIRP surgeon volume tertile				RRP surgeon volume tertile			
	Low $n = 211$	Medium $n = 34$	High $n = 11$	P value	Low $n = 879$	Medium $n = 236$	High $n = 86$	P value
Transfusion	3.1%	2%	1.4%	0.199	22.7%	21.3%	15.4%	0.017
Overall complication	22%	21.7%	21.7%	0.996	25.7%	25.6%	18.4%	<0.001
Cardiac	1.9%	2.3%	1.8%	0.805	3.5%	2.9%	3.2%	0.493
Respiratory	5.3%	4%	3.3%	0.336	8.2%	6.7%	4.9%	<0.001
Genitourinary	2.7%	1.6%	2.6%	0.339	1.6%	1.1%	1.1%	0.337
Wound	1.2%	<1%	2%	0.169	1.8%	2.1%	0.9%	0.004
Vascular	2.2%	4%	2.1%	0.255	4.4%	3.9%	3.2%	0.111
Miscellaneous medical	10%	10.6%	8%	0.610	10%	9.1%	6.9%	0.011
Miscellaneous surgical	4.5%	5.1%	3.9%	0.611	5.9%	6.8%	3.4%	<0.001
Length of stay†	2.2	2	1.8	0.061	3.6	3.3	2.9	<0.001
Stricture	6.1%	4.8%	5%	0.730	16.3%	15.6%	10.1%	0.003
Additional cancer therapy‡	7	4.7	4.5	0.020	7.1	6.8	5.7	0.044
Cystography	23.7%	22.2%	46.1%	0.146	9.2%	6.9%	13.9%	0.130

† Mean ratios.
‡ Rate per 100 person years, follow-up until 12/31/2006.

icant. Further, patients of high volume ORP surgeons were less likely to require additional cancer therapy ($P = 0.044$).

4. Discussion

Recently, a rapid shift in utilization from ORP to MIRP has occurred with more than 75% of radical prostatectomies being performed via robotic-assisted MIRP today [19]. While significant ORP surgeon volume-outcome effects have been shown [4,20], little is known about how MIRP surgeon volume affects outcomes outside of single institution studies, which have demonstrated prolonged learning curves for MIRP beyond 500 cases [21,22]. Furthermore, less is known if and how the volume outcomes effects for MIRP and ORP differ.

Our study has several important findings. First, men undergoing MIRP and ORP with high volume surgeons were less likely to receive additional cancer therapies, indicating better cancer control. Our population-based findings confirm previous work from single and multi-institution centers of excellence. Vickers found the predicted probability of recurrence at 5 years was 17.9% and 10.7% for men treated by ORP surgeons with 10 and 250 prior operations, respectively [20]. Vickers performed a similar analysis for non-robotic MIRP and demonstrated that prostate cancer recurrence decreased from 17% to 16% to 9% after surgeons had performed 10, 250, and 750 prior procedures, respectively [22]. Additional, a previous study using a different population-based cohort found that higher MIRP surgeon volume was associated with less need for additional cancer therapies [8]. The confirmation of these centers-of-excellence results with those from population-based studies allows for the confident generalization of findings.

Second, we observed significant ORP surgeon volume effects for certain peri-operative outcomes. Patients of higher volume ORP surgeons were more likely to experience shorter hospital stay, and fewer transfusions, 30-day complications and anastomotic strictures. These results recapitulate those from multiple previous studies from the urologic and general surgery literature [3,4]. Higher volume surgeons may possess a better understanding of the complex dorsal venous anatomy, and ability to limit excessive bleeding. Estimated blood loss (EBL) in ORP series range widely from 385 to 1,550 mL per case, resulting in a 4% to 55.7% ORP transfusion rate [23]. Studies have implicated EBL as a significant mediator of blood transfusions, hospital length of stay, and postoperative complications [24]. In addition, higher EBL has been associated with a higher risk of anastomotic stricture, presumably due to poor direct visualization because of bleeding or hematoma formation resulting in urinary leak and subsequent stricture [25]. Differences in EBL between high and low volume surgeons may be the main driver of differences in risk of transfusion, extended hospital stay, 30-day complications, and anastomotic stricture.

Third, we failed to identify MIRP surgeon volume-outcome effects for the peri-operative outcomes observed with ORP, suggesting that MIRP surgical technique affords some advantages that allow low vs. high volume MIRP surgeons to achieve similar peri-operative outcomes. One well-established benefit of MIRP is less variation in estimated blood loss (EBL) due to the tamponade effects of pneumoperitoneum [26]. EBL in recent MIRP series range from 50 to 380 mL [26], and the lower MIRP EBL may contribute to the absence of volume-outcome effects for these outcomes. In addition, during ORP anastomosis, it may be difficult to directly visualize posterior mucosal apposition, and securing the anastomosis is done mostly by feel, which requires significant experience. During MIRP, however, direct visualization of the anastomosis is afforded by the camera, which, in addition to the lower EBL, may explain the absence of a MIRP volume-outcome effect for anastomotic strictures in our population-based study. Furthermore, during intraperitoneal MIRP, mobilization of the bladder may further decrease tension, facilitating the anastomosis.

Our study must be interpreted in the context of the study design. First, administrative data are primarily designed to provide billing information, not detailed clinical information. However, Medicare administrative data have a high degree of validity for detecting in-hospital surgical complications [27]. Second, short-term prostate cancer survival is high, and lengthier follow-up is needed to assess differences in cancer control. There may be regional differences in utilization of adjuvant radiation for pT3 or margin-positive disease that may confound our findings. Third, our findings may not be generalizable to men $\leq$ 65 years, or those undergoing surgery outside of SEER regions. Finally, we were unable to differentiate MIRP with vs. without robotic-assistance, as both share a common CPT-4 code; however, the advent of robotic-assisted MIRP has led to a near disappearance of pure laparoscopic MIRP in the U.S. during our study period, especially in the community setting [28]. Therefore, the robotic-assisted approach likely accounted for the majority of MIRP in our study.

5. Conclusion

Men undergoing MIRP or ORP with high volume vs. low volume surgeons were less likely to require additional cancer therapies. Additionally, men of high volume ORP surgeons were more likely to avoid blood transfusions, experience shorter hospital stays, fewer 30-day complications, and less anastomotic strictures, while MIRP surgeon volume did not affect these peri-operative outcomes.

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Appendix

Type of outcome	Time after surgery	Category	Diagnosis codes	Procedure codes
Postoperative outcomes	0–30 days	Cardiac complication	ICD9: 410.xx, 402.01, 402.11, 402.91, 428.xx, 427.5, 997.1	
		Respiratory complication	ICD9: 518.0, 514, 518.4, 466.xx, 480.xx, 481, 482.xx, 483.xx, 485, 486, 518.5, 518.81, 518.82, 799.1, 997.3	
		Genitourinary complication	ICD9: 595.89, 590.1x, 590.2, 590.8x, 590.9, 591, 596.6, 593.3, 593.4, 593.5, 593.81, 593.82, 997.5, 596.1, 596.2	ICD9: 55.02, 55.03, 55.12, 55.93, 55.94, 59.93, 97.61, 97.62, 56.1, 56.41, 56.74, 56.75, 56.81, 56.84, 56.86, 56.89, 56.91 CPT: 50040, 50120, 50125, 50395, 50398, 50605, 52290, 52332, 52334, 50600, 50700, 50715, 50760, 50770, 50780, 50782, 50783, 50785, 50800, 50810, 50815, 50820, 50825, 50840, 50900, 50940
		Wound complication	ICD9: 567.xx, 998.3, 998.5x, 998.6	ICD9: 54.61, 54.1x, 54.91, 54.0, 59.19 CPT: 26990, 45020, 49060, 51080
		Vascular complication	ICD9: 415.1, 451.1x, 451.2, 451.81, 451.9, 453.8, 453.9, 997.2, 999.2, 444.22, 444.81, 433.xx, 434.xx, 436, 437.xx	
		Miscellaneous medical complication	ICD9: 584.xx, 586, 785.5x, 995.0, 995.4, 998.0, 999.4, 999.5, 999.6, 999.7, 999.8, 457.8, 560.1, 560.8x, 560.9, 997.4, 353.0, 354.2, 723.4, 955.1, 955.3, 955.7, 955.8, 955.9, 593.4, 531.xx, 532.xx, 533.xx, 782.4, 573.8	
		Miscellaneous surgical complication	ICD9: 599.1, 596.1, 596.6, 565.1, 569.3, 569.83, 569.4x, 998.1x, 998.83, 998.9, 998.2, 998.4, 998.7, 604.0, E870.0, E870.4, E870.7, E870.8, E870.9, E871.0, E873.0, E876.0, 956.0, 956.1, 956.4, 956.5, 956.8, 956.9, 902.50, 902.51, 902.52, 902.53, 902.54, 902.59	ICD9: 46.03, 46.04, 46.10, 46.11, 46.14, 48.4x, 48.5, 48.6x, 48.7x, 48.9x
		Blood transfusion		ICD9: 99.0x CPT: 86930, 86965, 86999 HCPCS: P9010, P9011, P9017, P9021, P9022, P9038, P9039, P9040
Anastomotic stricture	31–365 days		ICD9: 596.0, 598.9, 598.2	ICD9: 57.85, 57.92, 57.91, 58.1, 58.5, 58.6, 58.3x CPT: 51800, 53640, 52275, 52276, 52281, 52282, 52283, 52510, 53400, 53405, 53410, 53415, 53420, 53425, 53600, 53601, 53605, 53620, 53621
Long-term incontinence diagnosis	Greater than 18 months		ICD9: 788.3x	
Long-term incontinence repair	Greater than 18 months			ICD9: 58.93, 59.72, 89.21, 89.22, 89.23,89.24, 89.25 CPT: 51715, 53440, 53442, 53443, 53444, 51736, 53445, 51725, 51726, 51772, 51784, 51785, 51792, 51795, 51797, 51798, 51741
Long-term erectile dysfunction diagnosis	Greater than 18 months		ICD9: 607.84	
Long-term erectile dysfunction procedure	Greater than 18 months			ICD9: 64.94, 64.95, 64.96, 64.97 CPT: 54231, 54235, 54400, 54401, 54402, 54405, 54406, 54407, 54408, 54409, 54410, 54411, 54415, 54416, 54417 HCPCS: C1007, C1813, C2622, C3500, C8514, C8516, C8534, J0270, J0275, J2440, J2760, L7900
Additional cancer therapy	Anytime after surgery	Hormonal therapy		ICD9: 62.41 CPT: 54520 HCPCS: C9216, C9430, G0356, J0128, J3315, J9202, J9217, J9218, J9219, S0165, S9560
		Radiation therapy		ICD9: 92.2x CPT: 76965, 77301, 77305, 77310, 77315, 77331, 77371, 77372, 77373, 77399, 77401, 77402, 77403, 77404, 77406, 77407, 77408, 77409, 77411, 77412, 77413, 77414, 77416, 77418, 77421, 77422, 77423, 77427, 77431, 77440, 77499, 77520, 77522, 77523, 77525, 79300, 79440, 79999, 4201F, 4210F, 4165F, 79200 HCPCS: G0174, G0242, G0243